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Annotation

Melatonin: A New Probe in Psychiatric Investigation?

J. ARENDT

The pineal gland, Descartes' seat of the soul, was variously considered until recently as a somewhat mysterious vestigial organ, or simply a good neuroradiological marker. The former point of view arose partly out of ignorance and the curious mythical associations related to its function as a 'third eye' in some lower vertebrates. The latter is due to the calcification which is present in most adult human pineal glands.

During the last 25 years, the demystification of the pineal has proceeded with ever-increasing speed and volume of publication, although admittedly some of the publications only add to the mystery. Its most important physiological function in mammals appears to be the transmission of information about length of day (or photoperiod) in species whose seasonal cycles of, for example, reproduction, coat growth and behaviour are dependent upon photoperiod (Tamarkin *et al*, 1985). In some birds and lower vertebrates it is an important component of the circadian system, acting either as a coupling agent or as a central rhythm generator (Underwood 1977; Menaker *et al*, 1981). It may have modulatory effects on some circadian rhythms in mammals (Quay, 1970; Armstrong & Redman, 1985). All of these effects appear to be due to the rhythmic pineal secretion of the neurohormone melatonin (*N*-acetyl-5-methoxytryptamine).

Synthesis of melatonin

The mechanisms controlling melatonin production involve indoleamines and catecholamines, adrenergic receptors, cyclic adenosine monophosphate (AMP), methylation, light sensitivity, and central rhythm-generating systems, all of which are of considerable interest to psychiatrists, particularly those concerned with affective disorders.

The synthesis of melatonin proceeds via *N*-acetylation and subsequently *O*-methylation of serotinin (5-hydroxytryptamine) (Axelrod, 1974; Klein, 1985). All the various aspects of this pathway within the pineal are rhythmic. Pineal serotonin declines at night. Serotonin *N*-acetyl transferase increases 30–70-fold at night, at least in rodents, and is thought to be the major rate-limiting step in melatonin production. Hydroxy-indole-*O*-methyltransferase also may increase in activity at night. Stimulation of the night-time enzyme activity arises from post-ganglionic sympathetic nerves originating in the superior cervical ganglion. The transmitter appears to be noradrenaline acting via a β_1-adrenoceptor with some α-receptor involvement. Noradrenergic activity increases in the early dark phase and is coupled to an increase in β-receptor number towards the end of the light phase.

Melatonin production thus occurs essentially at night in all species, whether nocturnal or diurnal. The rhythm is endogenous (i.e. internally generated) and arises from the suprachiasmatic nucleus in the hypothalamus – a so-called central 'clock' generating many circadian rhythms (Moore & Klein, 1974). In a normal environment the rhythm is synchronised to the 24-hour day; synchrony is achieved by the light–dark cycle acting via the retina. In addition to setting the periodicity of the rhythm, light of suitable intensity will suppress melatonin production at night (Lewy *et al*, 1980) and in the appropriate circumstances serves to control the duration of the night-time peak (Arendt, 1986).

Most of this information was originally derived from work in animals. In humans, there is good evidence for most aspects of this pathway (Arendt, 1988).

Melatonin and affective disease

Abnormalities in circadian rhythms have been postulated (Wehr & Goodwin, 1983). Specifically, disruption of sleep, especially early waking, early-onset episodes of rapid eye movement (REM) and possible earlier timing of the cortisol and temperature rhythms are associated with endogenous depression. Diurnal variation in mood may also come into this category.

Periodic episodes of depression and mania, particularly the rapid-cycling variety, may relate to disorders of the time-keeping systems. An 'internal desynchronisation' hypothesis has been advanced whereby two central rhythm-generating systems with slightly different periods might generate a 'beat' phenomenon manifested as periodic clinical symptoms (Halberg, 1968, cited in Checkley, 1989).

The oscillatory structure of the circadian system is a matter for considerable debate; however, there is some evidence that the melatonin rhythm results from a strongly endogenous oscillator(s) also concerned with the generation of cortisol and temperature rhythms (Wever, 1986). Thus we might expect to find differently timed melatonin rhythms in unipolar and bipolar disorders if any of these ideas are correct. In general, this does not appear to be the case, with the possible exception of seasonal affective disorder (SAD or winter depression) (Lewy *et al*, 1987). There is undoubtedly some evidence for a decline in the amplitude of the melatonin rhythm in depression (e.g. Wetterberg, 1978; Claustrat *et al*, 1984; Frazer *et al*, 1986). This may reflect abnormalities of the circadian system, but other factors may be involved (see later) and not all studies are consistent (e.g. Thompson *et al*, 1988).

A non-uniform seasonal distribution of affective disorders has been known for some considerable time. It has been shown in large populations that the incidence of depression peaks in spring, with a secondary peak in autumn (Eastwood & Peacocke, 1976). One theory proposed to explain this phenomenon is related to the rapid change in length of day at these times. As the light–dark cycle is a major synchroniser of circadian rhythms it is possible that coupling of the circadian system is less robust at the equinoxes (Papousek, 1975), and indeed most particularly after the forced phase shift of artificial summer time.

If such is the case, then abnormal phase relationships within the circadian system should be demonstrable, for example, melatonin in relation to the sleep–wake cycle. No consistent observations have been made; however, it is conceivable that very small changes are present, and are important but extremely difficult to detect. The melatonin rhythm itself is highly reproducible within the same individual in the normal population (Arendt, 1988). Careful investigation of this reproducibility and its relation to other rhythms within individual patients would be worthwhile, if difficult to accomplish.

A further category of depression with a seasonal incidence is SAD: in fact these patients may well be bipolar in view of reported mild spring mania following winter depressive episodes (Checkley, 1989). The treatment originally proposed for this disorder was the creation of an artificial summer day length using three hours of bright full-spectrum light (Vitalite, 2500 lux) morning and evening (Lewy *et al*, 1982; Rosenthal *et al*, 1984). The 'melatonin hypothesis' predicted that such light treatment would shorten the duration of melatonin secretion, thus generating a summer day-length signal, by analogy with animal work. The light treatment appears to be efficient, even though the very existence of this syndrome is questioned by some and a major placebo effect has also been proposed. On the other hand it does not appear necessarily to work through melatonin. For example, light treatment in the middle of the day had no effect on the melatonin rhythm but induced remission of symptoms (Wehr *et al*, 1986). Checkley *et al* (1989) administered light treatments of different duration (three hours and one hour) morning and evening in such a way that an identical effect (delayed onset of secretion) was seen on melatonin, but only the longer duration of light was an effective treatment.

Rosenthal *et al* (1988) used a β-blocker (atenolol) to suppress melatonin secretion in SAD patients, but did not find a significant improvement in mood. However, atenolol has many effects other than suppression of melatonin, and the precise profile of secretion was unfortunately not assessed.

Another series of observations in a group of SAD patients suggested that the melatonin rhythm itself was delayed compared with that in normal subjects (Lewy *et al*, 1987). In animals, brief pulses of light are able to shift activity–rest cycles backwards or forwards in time depending on the time of the light pulse with respect to the individual's circadian clock (Elliot, 1981). Bright light in the morning in this group of patients shifted the delayed melatonin rhythm backwards to a more normal phase position and was more efficient than evening light in treating this group. The inference was made that the shift in melatonin may relate to the treatment efficacy. Indeed, these same authors (Lewy *et al*, 1985) have proposed phase-typing the melatonin rhythm of patients with possible rhythm disorder and using this information to design appropriate rhythm-shifting treatments (especially bright light). This approach is of considerable theoretical interest but remains an isolated observation. Moreover a number of other observations should be taken into account. Normal volunteers have a phase-delayed melatonin rhythm in winter compared with that in summer (Illnerova *et al*, 1985; Bojkowski & Arendt, 1988). Bright light will also shift the melatonin rhythm in healthy men but has little effect on mood (Broadway *et al*, 1987).

Pharmacological doses of melatonin at different times of day given to normal volunteers have not been shown to modify mood in a number of reports. One study, however, found that giving gigantic doses of melatonin during the daytime exacerbated depression in a small group of subjects (Carman *et al*, 1976). In contrast, when used as a possible treatment for jet-lag travelling eastward, evening melatonin administration (phase advanced) tended to improve mood, at the same time shifting the endogenous melatonin rhythm to an earlier phase position (Arendt *et al*, 1987).

Patients with SAD may have delayed, advanced, or normal melatonin rhythms such that when grouped they appear to compare well with the general population. However, we are still short of information in this regard (Checkley *et al*, 1988). So far there is little information as to the relationship of the melatonin rhythm to other circadian variables such as cortisol and temperature in the same individual with SAD, and the maintained overall structure of the circadian system may be of much greater importance than observations of a single rhythm such as melatonin. It is possible that light functions as a synchroniser to strengthen the coupling of the system at all times of the day. It remains debatable, however, whether good internal synchronisation of rhythms is important for well-being or not.

Melatonin and noradrenergic and serotoninergic function

Most pharmacological antidepressant treatments will increase the availability of catecholamines and/or serotonin, acting through uptake mechanisms, increased precursor, or inhibition of catabolism. A suggested functional deficiency in biogenic amine function has proved to be a highly productive hypothesis. Moreover, observations in depressed patients fairly consistently support a state of serotonin deficiency (Heninger *et al*, 1984). Functional deficiency of noradrenalin, serotonin, or both has the potential to lower pineal melatonin production. There are conflicting observations on this subject (e.g. Thompson *et al*, 1988) but the weight of paper probably favours decreased melatonin in depression (e.g. Wetterberg, 1978; Claustrat *et al*, 1984; Frazer *et al*, 1986). One report also suggests state-dependent higher levels in mania (Lewy *et al*, 1978). These phenomena are perhaps not surprising in themselves and looked at in another way they may also reflect abnormal coupling of circadian rhythms.

Of greater interest is the response of melatonin to different antidepressant treatments. Most monoamine oxidase inhibitors appear to increase production, as do several amine reuptake inhibitors and precursors (Wirz-Justice *et al*, 1980; Namboodiri *et al*, 1983; Cowen *et al*, 1985; Thompson *et al*, 1985; Oxenkrug *et al*, 1986; Franey *et al*, 1986; Demisch *et al*, 1986). The data are not yet consistent enough to suggest a link between an increase in melatonin production and efficacy of treatment but this possibility certainly merits exploration. Both 5-methoxypsoralen (Souetre *et al*, 1988) and destyrosine γ-endorphin (Claustrat *et al*, 1981) increase melatonin through unknown mechanisms and may have antidepressant activity. *S*-adenosylmethionine, and rolipram (a phosphodiesterase inhibitor) probably increase melatonin and have antidepressant activity (Checkley *et al*, 1987; Bell *et al*, 1988). The melatonin response may also serve to differentiate between the modes of action of different agents. For example, a single dose of DMI (desmethylimipramine, 100 mg dose at 16.00 h), primarily a noradrenalin uptake inhibitor, advances the onset of melatonin secretion in the evening in normal people, leading to a longer duration of secretion (Franey *et al*, 1986). A single dose of fluvoxamine a serotonin uptake inhibitor, does not alter the timing of onset, but increases the amplitude and duration of melatonin secretion in normal volunteers (Demisch *et al*, 1986; Skene *et al*, 1989, unpublished). It may be that the onset of secretion is dependent on availability of noradrenalin and the amplitude on the availability of serotonin in healthy volunteers.

Chronic DMI treatment (over three weeks) in depressed patients tends to increase the amplitude of secretion without effect on timing mechanisms (Thompson *et al*, 1985) whereas in normal volunteers an initial increase is followed by a return to baseline values ('down-regulation'; Cowen *et al*, 1985). These observations suggest that the control of melatonin secretion in depressed patients differs from that in normals. Some antidepressants are reported to delay circadian rhythms in animals (Wirz-Justice, 1983). There is little evidence for this effect in humans, in entrained conditions, using melatonin as a rhythm marker.

Melatonin production by the pineal gland can be suppressed by β^1-antagonists (Hanssen *et al*, 1977; Cowen *et al*, 1983): in consequence it has been suggested that peripheral melatonin levels reflect pineal and possibly central β-adrenoceptor status. One theory as to the mechanism of action of antidepressants considers that modification of receptor sensitivity or numbers (down-regulation) plays a role. Some studies (see above) suggest that the melatonin response to chronic DMI indicates down-regulation in normals but not in patients (Cowen *et al*, 1985; Thompson *et al*, 1985). The question arises as to whether peripheral, and in animals, pineal melatonin levels do indeed reflect β-receptor numbers either in the pineal, the central nervous system (CNS) (and where in the CNS) or both. Recent unpublished work from my laboratory (Franey, 1988) suggests that there is no simple relationship between pineal and cortex β-receptor numbers and pineal melatonin synthesis in rats treated with DMI for three weeks. This relationship in humans is obviously very difficult to explore, although post-mortem studies would be worthwhile.

Melatonin as a psychiatric probe

One area of promise using melatonin as a psychiatric probe is concerned with the light sensitivity of bipolar patients. The complete suppression of melatonin production in healthy volunteers at night requires rather bright light (2500 lux) (Lewy *et al*, 1980) although partial suppression may be achieved with 300–500 lux (Bojkowski *et al*, 1987*b*). Early reports suggest that in bipolar patients complete suppression may be achieved with 500 lux (Lewy *et al*, 1981). These observations require further confirmation. They may prove to be of both diagnostic and therapeutic importance. Familial sensitivity is currently being investigated as a possible genetic marker (Nurnberger *et al*, 1988). Lithium treatment appears to reduce light sensitivity in bipolar patients (Carney *et al*, 1988), hence this phenomenon may be strongly related to the manifestation of the disease. An involvement of biological rhythms is again suggested – possibly over-responsiveness of the circadian system to the unpredictable exposure to artificial light in domestic environments. In this area we must, however, tread with care – light sensitivity is determined by a number of factors and especially previous light exposure (Reiter, 1985). We will have most particularly to take into account people's lifestyles – outdoor workers see up to 100 000 lux on a sunny day, while office workers in winter rarely see more than 1000 lux (Okudaira *et al*, 1983).

Melatonin is now reliably measured by radioimmunoassay or GCMS. Assessment of its production does however require frequent blood sampling, usually over 24 hours. It is now possible to measure its major metabolite, 6-sulphatoxymelatonin, or aMT6s, by a robust and simple radioimmunoassay (Arendt *et al*, 1985; Aldhous & Arendt, 1988). Urinary aMT6s is a good index of both the timing and amplitude of melatonin secretion (Bojkowski *et al*, 1987*a*), although subtle changes in timing may be missed. It provides a useful, non-invasive tool for the assessment of melatonin secretion and makes this area accessible to anyone able to make urine collections.

Melatonin as a therapeutic agent

As a matter of personal opinion, I feel that melatonin has possible therapeutic potential in the treatment of mild depression and insomnia using timed, low-dose, oral treatment. It carries a licence from the US Food and Drug Administration for human use, although no substantial clinical trials have yet been reported. Certainly in the majority of individuals exogenous melatonin is effective in alleviating sleep disturbance, resynchronising the endogenous melatonin rhythm, and improving mood in jet-lagged travellers who have traversed eight or more time-zones (Arendt *et al*, 1987; Arendt & Aldhous, 1988). Its possible chronobiotic effects on sleep and its own rhythm are also emerging in studies in blind subjects with free-running circadian rhythms (Arendt *et al*, 1988; Sack & Lewy, 1988). Recently putative melatonin receptors have been described in the human SCN (Reppert *et al*, 1988), a central biological clock, thus providing an anatomical substrate for the phenomena described above.

This charismatic molecule with the melodious name is far more than a 'probe'. It may well serve to counter some of the lack of well-being attributable to the biological insults of civilisation.

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Information on the availability and price of assays for melatonin, its principal metabolite and related products can be obtained on application to the author.

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Annotation

Forensic Aspects of Mental Handicap

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Areas of need exist where people with a mental handicap experience problems greater than, or differing from, the rest of the population. For example, there is a greater than average incidence of psychiatric disorder in mentally handicapped adults (Heaton-Ward, 1977) and children (Rutter *et al*, 1970; Gath & Gumley, 1986). Also, their families experience greater psychological distress and require support in their own right (Dupont, 1986; Shulman, 1988).

It has long been claimed that the mentally handicapped have special forensic problems. This belief has been supported by archaic notions of moral degeneracy and social incompetence, which had been given credibility by the eugenics movement; this article examines the evidence for such a belief.

Legal definitions

The Mental Health Act 1983 defines mental impairment as "a state of arrested or incomplete development of mind including significant impairment of intelligence and social functioning in association with abnormally aggressive or seriously irresponsible conduct". Severe mental impairment is defined similarly, except that the impairment of intelligence and social functioning must be severe. Mental impairment is not defined in terms of IQ, and the Act lacks adequate definition of intellectual deficit. The significant practical consequence is that an individual cannot be detained or committed under the Mental Health Act on the basis of intellectual level alone: *social* functioning must also be impaired. Furthermore there must also be abnormal aggression or serious irresponsibility. Similarly, in the USA intelligence tests alone are not considered an accurate measure of handicap. There must also be inadequate adaptive functioning (Menninger, 1986).

In contrast, Bicknell (1987) advocates an operational definition. She argues that it serves a more useful purpose for day-to-day clinical needs than the above legislative terms: "someone can use our service if through developmental intellectual handicap he or she requires such special services as we provide to move closer to an ordinary lifestyle". This definition could be taken to imply that such a service should be confined to developmental handicap. It would be important to ensure that these facilities were available to someone who had become handicapped following say, a road traffic accident, wrongly applied anaesthesia, or the results of an extensive brain tumour resection.

The distinction between mental impairment and mental handicap is an important one. The term 'handicap' implies some disability or disadvantage. 'Mental impairment', as defined in the Mental Health Act 1983, can be applied only to a small subgroup of mentally handicapped people. Some idea of the degree of intellectual retardation is provided by the educational terms 'mild/severe learning disability' which have replaced the old categories of 'mild/severe educational subnormality'.

Epidemiology

Throughout the first half of the this century it was widely believed that an individual's intellectual level was inversely related to his likelihood of committing an offence. A direct association between mental handicap and criminality now seems far less likely. Social factors appear to be of great significance. Woodward (1954) reviewed relevant literature and found that the proportion of convicts with an IQ lower than 70 decreased as intelligence tests became more refined. Over time these tests had changed their emphasis from one of assessment of acquired education to one of assessment of practical abilities. These improved tests revealed that a considerably smaller proportion of individuals with an IQ less than 70 had been convicted of an offence. Woodward's findings are compatible with the much more recent notion that delinquency is associated with "cycles of disadvantage" (Rutter & Madge, 1976) rather than with IQ *per se*.

Prentice & Kelly (1963) found only slight differences in performance IQ between normal and delinquent individuals. They concluded that delinquency was largely unrelated to intelligence. However, there was a considerably lower verbal IQ among delinquents. This was explained by the authors as being indicative of learning disability. Ferracuti (1966), in a literature review, argued that progressive methodological improvements over time refute the concept that criminal behaviour derives from a low level of intellectual endowment. However, he also concluded that sexual offenders have a lower intellectual level, and that performance scores exceed verbal scores for psychopathic and criminal groups.

West & Farrington (1977), in their comprehensive epidemiological study, cite low IQ as an adverse background variable predisposing to delinquency. However, the case studies they describe make it clear that low IQ is only one of many factors, and is usually associated with multiple social variables, for example low parental income, large family size, poor parental behaviour, and parental criminality. The presence of a below-average IQ at age 14 was found to be a factor associated with juvenile delinquency, and was also predictive of early adult convictions. Many of these individuals, despite their low intellectual ability, would not be classified as mentally handicapped.

More recently MacEachron (1979) has found that the prevalence rate for mental retardation in adult male offenders is only slightly higher than the prevalence rate for mental retardation in adult males in the general population. Again, little support is forthcoming for a conceptual link between mental handicap and criminality. MacEachron concluded that social variables, for example aggression, inadequacy, homelessness, and a recidivist upbringing, were more important than IQ.

In contrast, Hirschi & Hindelang (1977), in a review of sociological research, conclude that IQ has an effect on delinquency independent of class and race, and that this effect is mediated through school variables. Similarly Moffitt *et al* (1981), in two prospective longitudinal studies, found a relationship between IQ and delinquency which is independent of the effects of socio-economic status. The authors suggest that children of low IQ are more likely to engage in delinquent behaviour because their poor verbal abilities limit their opportunities to obtain reward at school.

Reichel (1987) critically reviewed a large number of relevant studies and found consistently lower IQs for criminals than for non-criminals, but the difference in mean IQ points separating the two groups was roughly five to ten. This implies that the mean IQ of offenders is still usually located within one standard deviation of the population mean – well above levels usually recognised as being compatible with mental handicap. Furthermore, the longitudinal delinquency studies that Reichel cites confirm the importance of such social variables as impoverished communities, deprivation, and parental criminality.

In summary, a low intellectual level does indeed appear to be one of many factors predisposing to criminal behaviour. However, the presence of family, social, and environmental factors are of enormous importance, as is their interaction with intellectual ability.

Reasons for coming to court

The reasons for the mentally handicapped appearing in court may be divided into factors culminating in an increased frequency of offences (impulsivity, suggestibility, exploitability, desire to please) and factors leading to a greater likelihood of detection (poor at concealing actions, less likelihood of ready access to legal counsel, desire to please, poor resilience). Menninger (1986) emphasises the importance of impulsivity and the need for immediate gratification. However, Clarke *et al* (1985) propose increased suggestibility as the reason. Hence, the victim may be more likely to be led into petty crime, to be exploited, and to be cajoled into taking the most risky role. Furthermore he would be less successful at concealing his actions or getting away. The consequent increased risk of apprehension by the police makes assessment of the significance of prevalence rates problematic. Hirschi & Hindelang (1977) argue against these proposals. They claim that the notion of differential ability to avoid detection and differential official reaction on the basis of IQ are not supported by available evidence.

Also, the likelihood of confession increases where there is no access to legal advice. Craft (1984) describes the Confait case (Fisher, 1977) as highlighting the suggestibility of the mentally handicapped. In this case a mentally handicapped individual was convicted of the murder of a male transvestite and subsequent arson, having admitted to the above offences under police interrogation. Later awareness of this person's innocence prompted the Royal Commission on Criminal Procedure (1981). The Commission recommended that "officers should take particular care in putting questions to, and accepting the reliability of answers from, a person who appears to have a mental handicap. Police should have improved training to enable more ready recognition of mentally handicapped persons in order to allow early safeguards, investigations, and expert advice." The Commission emphasised the need to recognise the subject's degree of mental responsibility, particularly since he may not readily comprehend the phrases used to caution those about to be questioned. In this respect the Criminal Evidence Act 1984 is also of relevance, as it contains a section requiring a warning to be given to a jury when there is uncorroborated confessional evidence.

The handicapped person's reduced resilience when placed under psychological stress is also an important factor. He may be unable to cope with interrogation or custody. Anxiousness to please may produce an unwarranted compliance, with agreement to almost any suggestion if it is felt that this will produce the desired response. This emphasises the need for clear safeguards that are actively applied during police interrogation and court proceedings.

In contrast, those with autism have somewhat different reasons for committing offences or appearing in court (L. Wing, personal communication). The common reasons are: specific, circumscribed interest; inability to learn from experience; paranoid sensitivity; confusion or a change in routine, leading to an aggressive reaction; diminished understanding of moral issues; diminished empathy for others' feelings; diminished understanding of the deeper meanings of what other people say, or of what is happening.

Common offences

Hunter (1979) claims that the mentally handicapped are indeed more likely than others to be convicted of certain offences. He describes arson and sexual misdemeanours, usually exhibitionism, as offences perpetrated more frequently by mentally handicapped people than by others. Hunter interprets the sexual offences as probably reflecting difficulty in finding suitable sexual partners. There is also likely to have been diminished awareness and appreciation of the significance of the culprit's behaviour. The perceived high rate of such offences may be explicable partly in terms of sexual experimentation being more overt, and hence more upsetting to others. Nonetheless, the commitment rate for sexual crimes among the mentally handicapped remains greater than for other people, and more often results in a hospital order. The offence is usually indecent exposure; the offender is usually a passive, immature under-achiever.

Indecent assault is comparatively rare. It usually takes the form of a pathetic unplanned attack by a male known to the victim. Paedophilia is also thought to be uncommon and usually reflects the low mental age of the offender with adult physique and adult hormonal drives.

An unfortunate quirk of the Sexual Offences Act 1956 is that although it is unlawful for a male to have sexual intercourse with a severely mentally handicapped female (provided he was aware of her handicap), there is no similar legal safeguard against seduction of a severely mentally handicapped male by a member of the opposite sex. However, an attempt at intercourse could still be deemed a common law offence.

In reality mentally handicapped men tend to have a diminished sex drive, and more often than not their behaviour tends to be misconstrued. It is certainly no longer tenable to make a blanket statement that people with a mental handicap are sexually irresponsible. Craft & Craft (1982) marshal evidence to prove that "people with a mental handicap are no more at the mercy of their sex impulses than the rest of us". Gunn & Rosser (1987) give a comprehensive review of the area of sex and the law as it relates to people with a mental handicap.

Arson is the other commonly committed crime. This may be a childish prank, an attention-seeking device, or the result of frustration or anger towards another person. It may also be a cry for help.

Legal procedures

Craft *et al* (1985) list the alternatives to conviction open to a person with mental impairment under English law. A person may be deemed "unfit to plead" by a jury if he is technically severely mentally impaired. Requirements for this verdict are that the accused must be unable to understand the charge of the significance of his plea, or be unable to challenge a juror, or be unable to instruct counsel, or be unable to examine a witness, or be unable to follow the progress of the trial. Medical evidence needs to be advanced along the above lines to the effect that the person is "under disability" for the jury to reach this verdict. Under the Criminal Procedure (Insanity) Act 1964 that person becomes subject to an order with restrictions. The result can be admission to a special hospital, as decided by the Secretary of State for Social Services, until fit to plead. Alternatively the court can make an order under section 37 or section 41 of the Mental Health Act 1983, with or without recording a conviction. This requires a finding of mental impairment on medical examination. The result is hospital admission or reception into guardianship for six months unless renewed for a further six months (and then annually). Obviously imprisonment remains common, although a probation order, possibly with psychiatric treatment as a condition, may be preferable. In reality, the choice depends on the availability of treatment or training facilities in the vicinity, and whether the court demands residential placement for protection of the public.

Inadmissible evidence

Evidence can be excluded by a judge as inadmissible if the police have not taken special precautions with a known or suspected mentally handicapped person. Police interrogation should be during daylight hours, and should be in the presence of another person, such as a relative or social worker. Furthermore the times that the interview commenced and finished must be stated. If these criteria have not been fulfilled an adjournment can be requested to produce medical evidence on the client's suggestibility, the admissibility of his evidence, and the reliability of his interrogation. In the past evidence has been deemed inadmissible where the victim was interrogated alone following a midnight arrest. On another occasion the person was proved illiterate, although in his confession words had been used that were clearly beyond his comprehension. A confession has been deemed inadmissible because of the accused's signature having been appended where it was proved that he was unable to write, and also where a confession followed six hours in a small darkened cell.

Legislation for community needs

In contrast to the above restricting legislation, Gostin (1985) argues that legal efforts should be mandating or enabling. He states that efforts should be directed towards the needs of mentally handicapped people in the community, rather than towards the implicit equation of mental handicap with mental illness and psychopathy, as happens in the Mental Health Act 1983. Supporting this view is the fact that detention under this Act is usually due to concomitant psychiatric disorder, not the mental handicap itself. Legislation is seen as being needed for the individual's right to a home in ordinary housing, with safeguards to ensure acceptable standards of accommodation.

The Warnock report (1978) and the subsequent Education Act 1981 have ensured everyone's right to an education, irrespective of degree or nature of handicaps. The provision is on the basis of special educational needs with an official written statement if needed. In practice the Act enforces important safeguards. There is, however, the occasional ambiguity. Goacher (1987) points out a certain circularity: the Act states that a child has "special educational needs if he has a learning difficulty which calls for special provision to be made . . .' (s. 1, para. 1.).

The right to marriage and divorce needs to be respected. It must be remembered that those people detained compulsorily under a section of the Mental Health Act 1983 require leave from a responsible medical officer in order to marry. Gostin emphasises the need for freedom of sexual expression – an area ignored until recently, but now receiving increased attention (see Craft & Craft, 1982).

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Review Article

Drug Treatments of Dementia

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Present drug treatments for the more common types of dementia are largely palliative or symptomatic, but the promise of drugs to prevent the development of dementia does not seem unrealistic. Neuropharmacological strategies that aim to improve behavioural or cognitive symptoms in dementia are subdivided into drugs that modify central cholinergic, serotonergic, dopaminergic, GABAnergic, and peptidergic transmission. There are no clear clinical guidelines for the management of demented patients who are also hypertensive. The early identification of patients with incipient dementia, the detection of slight but theoretically important beneficial effects, the optimum method of drug administration, more soundly based treatment of behavioural symptoms, and the evaluation of drug combinations are all identified as areas requiring further research.

There is a compelling need for well conducted studies of the treatment of dementia. Major changes in the age structure of our population and consequent increases in the prevalence of all age-related diseases have placed a steadily growing burden on our capacity to provide satisfactory care for increased numbers of old people, particularly those who are demented. Recent advances in understanding the neurochemistry and the molecular biology of dementia are widely reported, and professional and public expectations of the potential benefits of such progress have understandably increased. Occasional reports of patients whose severe and apparently irreversible dementia recovers completely in response to therapy (e.g. Paulson, 1983) strengthen the hope that, eventually, specific treatments will become available for the more common forms of dementia. Among specialists in the care of old people, however, considerable pessimistic reserve about the treatment of dementia remains commonplace, yet it is clear to all concerned just what might be the rewards of even a slight degree of improvement or a moderate slowing of an otherwise relentless decline. For the patient in the early stage of a dementing illness, this might mean the difference between independence and in-patient care, while for the planner of health services it could translate into reduction in demand for hospital beds.

Treatment studies in dementia have not proved easy to design or to interpret. Demented patients often suffer from other medical disorders and, since many are more than 80 years of age, their treatment is complicated by age-related changes in the absorption, distribution, and excretion of drugs. Frequently there is poor compliance with drug regimes, worsened by any cognitive deficits. When other medicines are concurrently prescribed, it is often difficult to judge precisely whether an unwanted effect is a consequence of the new drug or is related to an intercurrent disease or is an unexpected drug interaction.

Attempts to treat dementia are not new and the history of medicine is replete with examples of failed treatment ventures. Recent optimism dates from important advances in the study of brain chemistry, especially those that related the degree of dementia to the extent of post-mortem neuropathological and neurochemical changes (Perry *et al*, 1978). From the outset, it was clear that the relative neglect of dementia as a topic worthy of systematic clinical inquiry meant that many well intended investigators were working without much-needed basic information. Firstly, there was ignorance about the precise nature of the symptoms of dementia, the extent to which the presence of one symptom depended upon another, and the exact progress of the disorder. This type of information was, and remains, crucial to planning treatment studies, especially where it is reasonably expected in the initial stages of drug development that the benefits of treatment may be only slight. Secondly, assumptions were required about the potential value of a specific treatment on a target symptom of dementia when the neurobiological basis of that symptom was unknown or where it seemed unlikely that a simple reductionist model of the nervous system would suffice. Higher-order cognitive abilities, including memory, are likely to involve numerous synapses and transmitters (Black *et al*, 1987) and although much recent research in Alzheimer's disease (AD) has emphasised the role of cholinergic cells, other neurotransmitter systems deteriorate in this condition and may be implicated in the cognitive deficits associated with dementia (Kopelman, 1985).

TABLE I

Neurotransmitter changes in Alzheimer's disease (AD), Huntington's disease (HC), alcoholic dementia (Alc), multi-infarct dementia (MID), Parkinson's disease (PD), and ageing in the absence of dementia

Transmitter	*AD*	*HC*	*Alc*	*MID*	*PD*	*Ageing*
Ach-CAT	↓↓↓	↓	↓	→	↓	↓
ACE	↓↓	↓	↓	→		→
DA	↓	↓	↓		↓	↓
NA	↓		↓	→	↓	↓
GABA	↓	↓	↓			↓
5-HT	↓↓	↑			↓↓	→
CRF	↓↓				↓	
NY		↑				
SS	↓					→
SP		↓				
GLUT	↓					→

ACh: acetylcholin, CAT: choline acetyl transferase, ACE: acetylcholinesterase, DA: dopamine; NA: noradrenaline; GABA: gamma amino butyric acid; 5-HT: serotonin; CRF: corticotrophin-releasing factor, NY: neuropeptide Y; SS: somatostatin; SP: substance P; glut: glutamate.

↓ decreased, ↑ increased, → unchanged or uncertain.

Adapted from Hardy *et al* (1985).

Neurochemical pathology of the dementias

From a neurochemical standpoint, AD is by far the most exhaustively studied of all the dementias, and there is a paucity of information about cerebrovascular or alcoholic dementia. The literature allows few valid comparisons between the subtypes of dementia, largely for technical reasons but also because the brain areas sampled may differ substantially from one study to another. Small study numbers often limit statistical treatments of data and, unfortunately, this is particularly true of cerebrovascular dementia, despite the fact that it is relatively common. Table I summarises major findings to date. It shows that the cortical cholinergic deficit is not unique to AD, that in most respects the subcortical changes in Huntington's disease (HD) are highly specific, and that in AD deficits occur in transmitter systems other than the cholinergic.

Two hypotheses, both relevant to treatment, are derived from studies of the neurochemical pathology of the dementias and these concern the specificity and selectivity of the neurotransmitter changes found in each type of dementia. The *specificity* hypothesis proposes that each dementia has its own characteristic pattern of neurotransmitter abnormalities. Detection of such disease-specific patterns of neurotransmitter changes during life would, of course, substantially improve the accuracy of the diagnosis of dementia, which would be invaluable to treatment studies. The *selectivity* hypothesis postulates that the pattern of neurotransmitter changes found in each type of dementia correlates closely with the exact pattern of neuronal loss. From a therapeutic standpoint, demonstration of a disease process that leads to selective neuronal loss raises possibilities that target neurons could be precisely identified by the pattern of transmitter changes and that a single factor, available to therapeutic manipulation, is responsible for the selective loss of neurons. This thought was certainly uppermost in the minds of clinicians treating the cholinergic deficit in AD.

Diagnosis and the measurement of change

The symptoms and signs of dementia include a mixture of deficits in learning and memory, language, and psychomotor speed. These are accompanied by varying degrees of impairment of reasoning, behavioural problems, attentional difficulties, movement disorders, and disturbances of temperament and mood (Huppert & Tym, 1986). The cognitive symptoms of dementia are central to most concepts of the disorder, and the behavioural and affective changes are seen as complications (Miller, 1981). This has potential relevance to treatment studies, since the alleviation of a primary symptom may lead to the relief of secondary symptoms. Demented patients can vary substantially in the nature and severity of such cognitive symptoms, attributable in part to the exact location of the pathological changes taking place in the dementing brain, and also to the fact that, as the pathology progresses, the dementia may worsen in a non-uniform manner. A sample might contain patients who have some functions well preserved yet others deteriorated seriously. Variability of the nature and severity of clinical features is commonplace in dementia of presumed vascular origin and discrepancies between behavioural and cognitive symptoms are often pronounced. Measures of change in treatment studies of dementia must be sensitive to a wide range of dysfunction and severity (Rosen *et al*, 1984), yet at the same time not demand too much of the cognitively impaired patient who may be unable to co-operate for more than 30 to 40 minutes. There are as yet no measures of change that are entirely satisfactory in these respects.

An important aspect of most if not all of those neurochemical studies of dementia that provided the springboard for much of the current therapeutic optimism is that they have relied (quite properly) on precise neuropathological confirmation of clinical diagnoses. Unfortunately, the same is not true or even possible for the clinical studies that seek to capitalise on these advances. Since most clinicians are understandably wary of an invasive validatory procedure like cerebral biopsy when the possible gains for a particular patient seem slim, almost all treatment trials are based on diagnostic criteria derived from clinical examination, with well recognised and potentially quantifiable risks of misdiagnosis. In this setting, a novel drug whose actions have been precisely anticipated by careful neurochemical investigations of diagnostically homogeneous groups of demented patients may fail to show an expected effect (especially when the effect is small) because treated patients could not be as reliably ascertained, thereby diluting and rendering statistically non-significant any advantage the new drug may in fact possess. It is among patients with senile dementia, who are the largest group likely to benefit from new treatments, that the problem of misdiagnosis is probably greatest. Cerebrovascular disease so commonly confounds Alzheimer's neuropathological changes in this group that it is often difficult, even when histological findings are to hand, to determine precisely the neuropathological basis of the clinical presentation. It is, therefore, mandatory for all drug treatment trials in dementia to state their diagnostic criteria and to ensure that, whenever possible, diagnoses are validated using neuropathological findings.

A further source of difference between studies in neurochemical pathology of the dementias and current neuropharmacological investigations concerns the stage of illness at which subjects are included. Neurochemical studies are based almost entirely on brain tissue obtained from patients dying in the terminal phase of illness, although it is clear from the few biopsy studies that the same neurochemical changes are present earlier in the course of the disease (Sims *et al*, 1980). However, drug treatments are probably more likely to be effective when used in patients with only a mild degree of dementia, in whom it is thought neurons have survived in numbers sufficient to respond to the treatment. Unfortunately, diagnostic criteria for mild dementia validated by natural history and pathological findings are not yet available, and there are difficulties in distinguishing mild dementia from the effects of coexisting physical illnesses, unrecognised depressive disorders, and 'benign senile forgetfulness' (Bergmann *et al*, 1971; Karl, 1978; Henderson & Huppert, 1984). Preliminary data from longitudinal studies are now beginning to appear in the literature and suggest that mild senile dementia of the Alzheimer type can be distinguished from health. In one recent study, subjects with mild memory impairment frequently progressed to AD, which was sometimes confirmed at autopsy (Rubin *et al*, 1989).

Neuropharmacological strategies

(a) Cholinergic

Alzheimer's disease

Early attempts to enhance the recovery of motor function following destructive cortical lesions often examined the administration of cholinergic drugs (Ward & Kennard, 1942). Although some benefits were detected in primate models, 'cholinergic stimulation therapy' never became an established clinical practice. In the modern era, interest in the possible benefits of cholinergic drugs in dementia dates from the demonstration that blockade of central cholinergic transmission by scopolamine in healthy volunteers causes a dementia-like syndrome, reversible by physostigmine, an anticholinesterase (Drachman & Levitt, 1974; Drachman, 1977). Later, the activities of enzymes associated with central cholinergic function were found to be decreased in brain tissue from AD patients (Davies & Maloney, 1976), and these reductions were found to be closely correlated with the density of senile plaques and deficits in cognitive function (Perry *et al*, 1978). Central cholinergic activity can be enhanced in health by administration of the acetylcholine precursors choline or phosphatidylcholine, which increase brain acetylcholine and cholinergic transmission (Cohen & Wurtman, 1975; Ulus & Wurtman, 1976) and decrease abnormal involuntary movements (Davis *et al*, 1976).

The cholinergic hypothesis has prompted much research, but is now seen to rest with some uncertainty on assumptions that an intact central cholinergic system is a prerequisite of normal memory, and that the signs and symptoms of AD are attributable to decreased central cholinergic function.

Although some early open studies suggested that supplementation of dietary choline (with choline or phosphatidylcholine) was of benefit in AD (Levy, 1978), more systematic studies provided no support for this conclusion (Bartus & Dean, 1982; Bartus *et al*, 1985; Little *et al*, 1985; Hollander *et al*, 1986). Little *et al* (1985) suggested that a subgroup of patients did in fact improve on long-term therapy, and that their improvement may have been more likely if compliance was poor. Their inference from these observations is that there is a 'therapeutic window' for the optimum dose of dietary choline, and this should be taken into account when planning future studies.

Physostigmine produces the most consistent improvements in both healthy volunteers (Davis *et al*,

TABLE II

Summary of reports on the effects on memory of physostigmine (occasionally used in combination with phosphatidylcholine) in demented patients

Reference	*Subjects*	*No.*	*Dose*	*Effects on memory*
Davis *et al* (1978)	volunteers	19	1 mg.i.v.	enhancement
Davis *et al* (1979)	dementia	6	0.125–0.5 mg.i.v.	modest improvement
Muramoto & Sugashita (1979)	dementia	1	1 mg.s.c.	improved constructional
Peters & Levin (1979)	AD	5	0.008 mg/kgBW s.c.	+ lethicin:improved
Smith & Swash (1979)	AD	1	1 mg.s.c.	some benefit
Christie *et al* (1981)	AD	11	0.25–1 mg.i.v.	some improved
Davis & Mohs (1982)	AD	10	0.125–0.5 mg.i.v.	some improved
Davis & Mohs (1983)	AD	13	2–8 mg oral	slight effects
Jotkowitz (1983)	AD	10	10–15 mg oral	nil effect
Thal *et al* (1983)	AD	12	3–6 mg oral	some improved
Welstein (1983)	AD	8	3–10 mg oral	nil
Mohs *et al* (1985*a*,*b*)	AD	12	4–16 mg oral	slight effects
Thal *et al* (1989)	AD	10	2–4 mg oral	some improved

All but one report concerns patients with a presumed diagnosis of Alzheimer's disease. Davis *et al* (1979) included three non-demented elderly patients, one Huntington's disease and two with Alzheimer's disease.

1978) and in AD (see Table II). Although enhancement of attention by physostigmine may partly explain improvements in memory, drugs that only improve attention do not improve memory performance in AD. The incidence of unacceptable peripheral effects, a short half-life and a narrow therapeutic window, the slight degree of improvement, and the fact that only a minority of AD patients improve after physostigmine have tempered enthusiasm for its use in AD, and encouraged the development of cholinesterase inhibitors. Latterly, intense interest centred on tetrahydroaminoacridine (THA) after the report by Summers *et al* (1986) of substantial gains by AD patients after treatment with THA. The study has encountered many methodological criticisms (Pirozzolo *et al*, 1987; Tariot & Caine, 1987) and a follow-up multicentre trial was temporarily halted by the United States Food and Drug Administration for assorted reasons, including reports that 20% of the first-treated patients had some hepatic impairment (Marx, 1988).

The use of cholinergic agonists in AD has not been widely investigated, largely because of their side-effects and lack of selectivity for central neurons. Pilocarpine was found to be ineffective in AD by Caine (1980), but the first study of physostigmine and arecoline in AD (Christie *et al*, 1981) provided some encouragement for further studies. The Sandoz compound RS-86 (a cholinergic agonist) lacked efficacy (Bruno *et al*, 1986), and Davis *et al* (1987) found the muscarinic agonist oxotremorine to be without effect. Tariot *et al* (1988) administered in a double-blind randomised design 1, 2 and 4 mg/h arecoline to 12 patients with AD. As in the study of Christie *et al* (1981), no statistically significant enhancements of cognitive function were detected, but at the lower dose improved picture recognition was found. The study design of Tariot *et al* (1988) is of particular interest because of the care with which the investigators sought to demonstrate that the administered drug in fact produced central cholinergic activation. The authors argued that their observations of a combination of increased heart rate, lowered body temperature, and increased plasma cortisol concentrations with unchanged prolactin secretion were consistent with increased central cholinergic activation rather than the effects of stress.

At present, most available drugs that can be used safely to modify central cholinergic transmission have been tried in AD. The benefits of physostigmine remain the only consistent and relatively uncontroversial finding. Novel, longer-acting, and safer cholinomimetic drugs are confidently promised, and these may soon be available for clinical investigation. Perhaps, as initially suggested by Christie *et al* (1981), future clinical trials will select for inclusion in long-term studies only those AD patients who show a response to a shorter-acting drug, such as physostigmine. The lack of selectivity of available muscarinic agonists for M_1 or M_2 receptors (which exert functionally opposite effects) is currently the focus of some research.

Alcoholic dementia

The cholinergic hypothesis of memory impairment has recently been convincingly extended from AD to include the dementia associated with alcoholism. Among alcoholics there is a spectrum of psychological deficits that ranges from Korsakov's syndrome (KS) to milder forms of cognitive dysfunction. However, use of the term 'alcoholic dementia' to distinguish some cognitively impaired alcoholics from those with typical KS is not universally accepted. Tarter & Alterman (1984) and Goldstein (1985) concluded that the neuropsychological and presumed causal factors (alcoholic neurotoxicity, malnutrition, hepatic impairment, head injury, etc.) are so diverse in the non-KS group that it is unreasonable to regard alcoholic dementia as a discrete clinical entity. The outcome of cognitively impaired alcoholics is probably non-uniform, and the diagnostic requirements for alcoholic dementia are not simply the criteria for alcohol dependence combined with those for a steadily progressive dementia developing after long-term, excessive intake of alcohol. In the most thorough study so far, Cutting (1978) reviewed the case notes of 183 Bethlem and Maudsley in-patients with a final diagnosis of alcoholic psychosis and used these and interview data to examine the relationships between several categories of chronic organic mental deterioration and KS. He proposed that the spectrum of cognitive impairments in alcoholism included: (a) KS, which arose abruptly in alcoholics who were already mildy impaired, in whom nutritional deficiencies (particularly thiamine) appeared to be causally important and which tended to be irreversible; (b) alcoholic dementia, in which psychological deterioration developed gradually, appeared to be relatively independent of nutritional factors, and tended towards gradual improvement; (c) a mixed group of KS superimposed on alcoholic dementia. This classification should prove to be of value in future treatment studies of related memory impairments.

Thiamine deficiency has been consistently and clearly demonstrated as the important causal factor in the pathology of Wernicke's encephalopathy, even when it is not associated with alcoholism (Sable & Gubler, 1982). These pathological changes most frequently affect the grey matter around the third ventricle and brain stem, where demyelination and glial proliferation are characteristic. In KS, the medial dorsal nucleus of the thalamus, medial pulvinar and mamillary bodies are particularly involved (Victor *et al*, 1971) and, even when KS is not suspected ante-mortem, this type of pathological change is probably common place in alcoholics (Harper, 1983). The neurological signs of Wernicke's encephalopathy respond well to thiamine treatment, but the same is not true of the memory impairment. This may be because the brain has been irreversibly damaged by thiamine deficiency or because the memory impairment is caused by some other factor, such as alcohol neurotoxicity. The neurochemical pathology of KS is yet to be systematically described (McEntee *et al*, 1984) and so does not so far provide a rational basis for the therapy of memory deficits. Early reports of decreased indices of noradrenergic activity in KS (McEntee & Mair, 1978; Mair & McEntee, 1983) led to a study showing memory enhancement after clonidine, an alpha-2 adrenoceptor agonist, but not methysergide or *d*-amphetamine (McEntee & Mair, 1980). The memory deficits of alcoholism are, however, probably not attributable to damage to subcortical noradrenergic systems, but instead point to impaired central cholinergic function (Lishman, 1986).

A recent test of the cholinergic hypothesis of alcoholic dementia has provided evidence that the memory impairment associated with high alcohol intake is associated with decreased cholinergic function (Arendt *et al*, 1988). In this study, working and reference memory errors were induced in rats by high alcohol intake. These memory deficits were reversed about seven weeks after implants of cholinergic-rich foetal cell suspensions, and the extent of improvement correlated closely with the acetylcholine content, but not the noradrenaline content, at the implant site. Histology did not detect lesions in the periventricular grey matter of the alcohol-treated rats typical of KS, and so led the authors to question the widely accepted view that such lesions are causally important in the memory dysfunctions seen in this condition. The results of this study point to the possibility of investigating the effects on cognitive function in alcoholics with memory deficits of drugs that enhance central cholinergic activity (Lishman, 1986).

(b) Dopaminergic

Once the safety and efficacy of antipsychotic drugs had been demonstrated in younger patients, the behavioural problems of dementia were soon treated with the newly discovered antipsychotic drugs. Using a double-blind, cross-over design, Seager (1955) compared chlorpromazine and placebo in a diagnostically mixed sample of female patients (dementia, 29 subjects; schizophrenia, 12 subjects; depression, 6 subjects). Irrespective of diagnosis, nursing problems were much reduced in about 60% of patients on chlorpromazine but not on placebo. Later studies (Hamilton & Bennett, 1962*a*,*b*; Sugerman *et al*, 1964) added to these early findings, and in due course the use of antipsychotic drugs became an established part of clinical practice and their use is now almost routine.

The use of dopaminergic blocking drugs in the elderly is not yet well founded on substantial clinical investigations, and there are no clear-cut clinical guidelines. Recent reviewers (Helms, 1985; Risse & Barnes, 1986; Raskind *et al*, 1987; Sunderland & Silver, 1988) have remarked on the paucity of good studies, often finding problems in design, diagnostic criteria, measures of change and duration of treatment. In fact, Helms (1985) considered only three trials met all his methodological criteria, although this is probably too restrictive a view upon which to base clinical practice. The main findings of the study by Barnes *et al* (1982) are of interest. They could detect little difference between thioridazine, loxapine, and placebo after eight week's treatment of behavioural disturbance in 34 demented patients, and concluded "many older demented patients with behavioural disturbances are not significantly helped by ongoing antipsychotic treatment". Similarly, Petrie *et al* (1982) found that only about a third of actively treated (haloperidol or loxapine) demented patients improved. Obviously, such reported lack of efficacy is of some concern, especially since so many of the institutionalised elderly are regularly prescribed neuroleptics, often with anti-Parkinsonian medication (Michel & Kolakowska, 1981; Mann *et al*, 1984). Further, two of these studies (Rada & Kellner, 1976; Barnes *et al*, 1982) reported high placebo responses, strengthening the view (Hanley *et al*, 1981) that behavioural or non-pharmacological treatments should continue to be systematically evaluated in demented patients.

There is also a need for investigations on the effects of antipsychotic withdrawal. Fifty demented patients who had received chlorpromazine for at least seven months were changed to placebo by Barton & Hurst (1966), who noted little deterioration during the following three weeks. Although the authors concluded that some patients may receive neuroleptics unnecessarily, this was not clearly established as three weeks could be too short a period to recover from the effects of long-term administration.

The optimum choice of dopaminergic blocking drug for use in the elderly is not yet established. Reduced central cholinergic transmission in AD could lead to more frequent and severe anticholinergic side-effects of dopaminergic drugs like thioridazine, although this does not appear to be a common clinical problem and the practice of preferring neuroleptics with fewer anticholinergic effects (e.g. pimozide; Kushnir, 1987) has not been widespread. There is also some evidence that the dose range usually associated with the antipsychotic actions of dopaminergic blocking drugs is much higher than the dose range required by demented patients. Steele *et al* (1986) examined the effects of haloperidol and thioridazine on behavioural symptoms in 16 patients with senile dementia of the Alzheimer type, but only six patients completed the open, cross-over design. Both drugs were effective and although thioridazine was better tolerated, increased doses in two patients were associated with cognitive deterioration. Very low doses of haloperidol or thioridazine were used in two patients with dementia who had failed on conventional low-dose regimes but later showed clinical improvement on very low doses (haloperidol 0.125 mg daily or thioridazine 10 mg daily). Although a lower preferred dose of neuroleptic may reduce the incidence of unwanted effects, a survey of tardive dyskinesia studies led Kane & Smith (1982) to conclude that increasing age and female sex are the major risk factors for tardive dyskinesia, and that dosage, duration, and 'drug-free' periods do not reduce their likelihood.

In summary, the typical or 'core' symptoms of dementia (dysmnesia, disorientation, confusion, etc.) are not significantly changed by neuroleptics, and specific behavioural target symptoms must be present if these drugs are to be effective. These symptoms are well described by Reisberg *et al* (1987), who have also devised a rating instrument that may prove useful in future clinical trials.

Animal models of the behavioural problems that follow brain injury (Marotta *et al*, 1977) have prompted the use of dopaminergic agonists in comparable clinical settings, although as yet without success (Gualtieri, 1988). In elderly patients, drugs that potentiate dopaminergic transmission have rarely been considered other than in the setting of Parkinson's disease, where *l*-dopa was found to be ineffective in the treatment of cognitive symptoms in the absence of Parkinson's disease (Jellinger *et al*, 1980). The dopaminergic agonist memantine (20–30 mg i.v. *p.d.*) was thought ineffective by Fleischhacker *et al* (1986) in a placebo-controlled, single-blind study of 20 demented patients.

(c) Noradrenergic

The majority of research reports on the pharmacology of memory function in elderly subjects have involved manipulation of central cholinergic transmission. There is some evidence, however, that loss of catecholaminergic neurons contributes to cognitive decline in AD. Concentrations of noradrenaline, dopamine, and their metabolites are reduced in cortical tissue from AD patients to a greater extent than is found with ageing in the absence of dementia. Pharmacological enhancements of catecholaminergic function may, therefore, improve some of the symptoms of AD when used either alone or, potentially, in combination with cholinomimetic agents.

Arnsten & Goldman-Rakic (1985) conducted careful studies on the effects of ageing on cognitive performance tasks in rhesus monkeys. Clonidine, an alpha-2 adrenoceptor agonist, improved performance in each of five monkeys tested, and although at high doses (0.05–0.07 mg/kg) clonidine's sedative actions impaired performance, once an animal could tolerate this effect, similar improvements were observed. Unlike propranolol, which was without effects, yohimbine worsened performance, supporting the view that alpha- rather than beta-adrenoceptors are involved. Further studies showed that these actions are probably (a) unrelated to the sedative action of clonidine, as they could not be produced by diazepam, (b) mediated through alpha-2 adrenoceptors, as they could be prevented by the receptor antagonist, yohimbine, and (c) required the presence of adrenoceptors in the principal sulcal region. In the light of these results, Arnsten & Goldman-Rakic (1985) argued that since adrenoceptors do not appear to be reduced in AD (Hardy *et al*, 1985), therapy with adrenergic agents might prove of value in this disorder. Chronic therapy at high doses may be required in some subjects if the strategy is to be effective. Patients with KS show some improvement in memory after clonidine (Mair & McEntee, 1986). However, when eight patients with clinically diagnosed AD were studied in a double-blind, placebo-controlled trial of clonidine given orally (0.1, 0.2 and 0.4 mg), the drug was without effect (Mohr *et al*, 1989). Cognitive function was measured using alternative forms of object naming, verbal learning, sentence memory, word fluency, digit span, and visual retention. The authors concluded that "single neurotransmitter replacement therapies increasingly suggest the necessity for consideration of a multiple-system approach for the symptomatic treatment of Alzheimer's disease".

There have been few systematic trials of noradrenergic therapies in dementia. Most studies have examined the value of antidepressant drugs, although the reasoning has rarely been as well argued as in the above animal studies. The possibility that the behavioural problems of dementia may be responsive to monoamine oxidase inhibitors (MAOIs) was first suggested by the efficacy of MAOIs in hyperactive children (Zemektin *et al*, 1985) and discussed by Jenike (1986). Later, Tariot *et al* (1987) administered *l*-deprenyl, a selective monoamine oxidase B (MAO-B) inhibitor, to 17 Alzheimer patients in a double-blind, placebo-controlled, cross-over study in which placebo was followed by active drug (10 mg daily rising to 40 mg daily) later replaced by placebo. Improvement was observed in mean behavioural and cognitive scores, so much so that six of the 17 were thought to be "definitely improved", and this was more marked at the lower dose. Within the limitations of their design, the authors postulated that the greater efficacy at the lower dose pointed to inhibition of MAO-B and not MAO-A, and that selective "improved modulation" might play a neuroprotective role in AD. Their results suggest that *l*-deprenyl may prove of value in dementia.

There have been several reports that propranolol may be useful in the treatment of behavioural disorders associated with chronic organic cerebral disease. Elliot (1977) thought the aggressive behaviour linked to brain damage could be controlled by propranolol, and a few methodologically limited studies have tended to support this view (Schreier, 1979; Yufodfsky *et al*, 1981; Petrie & Ban, 1981; Williams *et al*, 1982). The mode of action of propranolol when used in the treatment of behavioural difficulties is unclear. Many of the patients chosen for study appear to have been unresponsive to more conventional treatments, and their symptoms may have been worsened by anxiety linked to the retention of some insight into their predicament. The efficacy of propranolol may thus be attributable to its anxiolytic effects, although the general lack of efficacy of benzodiazepines when used in this context would not support this view.

(d) Serotonergic

Potentiation of serotonergic transmission has recently been investigated in the treatment of behavioural and cognitive symptoms of dementia. The finding that post-mortem cortical tissue concentrations of serotonin are reduced in AD formed the basis of these studies, but several had been prompted by the clinical observation that the behavioural symptoms can be substantially relieved by antidepressants. O'Neil *et al* (1986) reasoned that since decreased brain concentrations of serotonin and its metabolites are associated with aggression in some animal models, combination treatment with tryptophan and trazodone might be effective. The same combination was later found useful in reducing the screaming and banging of an elderly demented patient (Greenwald *et al*, 1986). Systematic evaluation of this strategy in the management of behaviour disorders in dementia is awaited with interest. Alaproclate, a potent and selective blocker of serotonin uptake in central serotonergic neurons, was found to be ineffective in senile dementia (of either presumed Alzheimer or multi-infarct types) by Dehlin *et al* (1985). Likewise, Cutler *et al* (1985*a*) found zimelidine (also a serotonin uptake inhibitor) to be ineffective.

(e) GABAnergic

The pharmacological treatment of behavioural symptoms associated with dementia has been based on the sedative actions of a wide range of compounds and not on the specific activities of drugs acting on the underlying pathological processes. Optimum clinical management must take into account frequently expressed and persistent anxieties about needless overprescribing and the potential for harm of psychotropic drugs in old people (Castleden *et al*, 1977; Morgan *et al*, 1982; Gilleard *et al*, 1983).

Sedative drugs that are active at GABAnergic synapses are largely contraindicated in the care of demented patients. The induction of tolerance, worsening of confusion, and overall impairments of performance have contributed to this view. Chlormethiazole, which has anticonvulsant, hypnotic, anxiolytic, and sedative properties, is a notable exception to the general rule. It is widely used in the treatment of behavioural problems of old people, whatever the presumed cause. The neuropharmacology of chlormethiazole is not understood, but as it enhances the inhibitory effects of gamma-aminobutyric acid (GABA) and may also potentiate the effects of glycine, these seem the most likely bases of its actions. Because sleep disturbance commonly coexists in the demented elderly with other behavioural problems, the use of chlormethiazole has been extended to include the management of agitated confusional states where there is nocturnal wakening. Chlormethiazole is most often used as an hypnotic when the choice in the elderly is influenced by concern that their use, especially if prolonged, might worsen the cognitive or behavioural problems of dementia. The available literature supports the view that chlormethiazole has distinct advantages over the benzodiazepines (Bayer *et al*, 1986; Pathy *et al*, 1986) but is less helpful concerning other hypnotics. Controlled clinical trials have shown that chlormethiazole has advantages over haloperidol (ter Haar, 1977) and thioridazine (Ather *et al*, 1986), attributable to a lower frequency of side-effects.

Sarter *et al* (1988) suggested that a fresh look at GABAnergic antagonist therapies in AD may well prove fruitful. Firstly, they cite anatomical and pharmacological evidence that inhibitory GABAnergic neurons control the activity of basal forebrain cholinergic cells, thought to be involved in AD. Secondly, they suggest that GABAnergic antagonist drugs may disinhibit surviving cholinergic neurons in AD, and so enhance memory function. In support of their hypothesis they point to animal studies indicating that the amnesic effects of scopolamine can be attenuated by GABAnergic antagonists, which probably improve memory largely by improving acquisition (Gamzu, 1988). Like other hypotheses linking neurochemical changes to cognitive function, the reasoning may appear simplistic but it seems likely to stimulate further examination of the GABAnergic system in AD (Robbins, 1988).

(f) Peptidergic

Most if not all the neuropeptides of the cerebral cortex may coexist with classic transmitters and subpopulations of cortical neurons can be defined by the presence of particular peptides. In AD, there is a consistent decrease in somatostatin and corticotrophin-releasing factor (CRF) in the cerebral cortex, but other peptides are not affected. Importantly, these include neurohypophyseal peptides, vasopressin and oxytocin, putatively involved with memory, and vasoactive intestinal polypeptide that is found with cortical cholinergic neurons. Changes in receptors for somatostatin and CRF are markedly different in AD, somatostatin receptors decreasing by about 40–60% while CRF receptors increase.

Neuropeptides are found in almost bewildering variety throughout the central nervous system, although at concentrations often considerably below those of 'classic' neurotransmitters. Outside the hypothalamic–pituitary system, their functions remain almost unknown, despite more than a decade of intense inquiry. Presently, the non-endocrine actions of neuropeptides are believed to be as neurotransmitters, neuromodulators, and neurotrophic factors. Their relevance to treatment studies in dementia is based on two lines of argument. Firstly, some neuropeptides are thought to be important in the acquisition of adaptive behaviour. Since these involve learning, memory, attention, and motivation, they may be improved by treatment with those peptides. A successful therapy could include a neuropeptide chosen because of hypothesised 'behaviour enhancement' and not simply because it was decreased in post-mortem studies. Trials with analogues of ACTH and vasopressin and opiate receptor blockade are examples of this approach. Secondly, selective loss of neurons, believed to occur in some types of dementia, may be caused by a deficiency of a single peptide, especially if that peptide had a key part to play in the trophic functions of those neurons. Attempts to correct such an hypothesised deficiency with a somatostatin analogue (e.g. L363,586) as reported by Cutler *et al* (1985) exemplify this approach. Likewise, thyrotrophin-releasing hormone (TRH) is reported to enhance central cholinergic function (Yarbrough, 1979; Yarbrough & Pomara, 1985), and its use in motor neuron disease prompted its advocacy in AD. Subsequently, Peabody *et al* (1986*a*) assessed 300–500 μg TRH i.v. in four demented patients and found no effect..

Potentially, the neurotrophic protein nerve growth factor (NGF) is of considerable relevance to treatment studies in dementia. Elegant animal studies had already demonstrated the treatment potential of NGF following lesion experiments, and septo–striatal cholinergic neurons were known to be responsive to NGF before Fischer *et al* (1987) found that continuous NGF intracerebral infusions over four weeks were partially able to reverse cholinergic cell body atrophy and to improve spatial memory performance in aged rats. Previously, Hefti & Weiner (1980) had hypothesised that in AD, the loss of forebrain cholinergic neurons may be caused by a disorder of the trophic functions of these cells, reversible by treatment with NGF, and that this treatment may lead to clinical improvement. Cholinergic cell bodies in brain areas known to be affected in AD have cell surface receptors that can recognise NGF (Rosenberg *et al*, 1987), and this may be related to the selective vulnerability of these neurons in AD (Perry, 1988). Studies on the effects of NGF in AD are awaited with interest.

Vasopressin

Vasopressin and some of its synthetic analogues improve animal learning and memory (de Wied, 1976), and this may be related to the involvement of vasopressin in the integration of behavioural, neural, and hormonal components of stress responses (Koob *et al*, 1984). Vasopressin nasal spray improves memory in non-demented adults (Legros *et al*, 1978), effects that are probably independent of the endocrine actions of vasopressin since they can also be produced by its synthetic analogue 1-desamino-8-D-arginine vasopressin (DDAVP) that is largely devoid of its endocrine actions (Weingartner *et al*, 1981*a*). Early studies in dementia (Weingartner *et al*, 1981*b*; Durso *et al*, 1982; Tamminga *et al*, 1982) and cognitive impairments after head trauma (Oliveros *et al*, 1978; La Boeuf *et al*, 1978) were fairly encouraging. However, the most systematically conducted study to date (Peabody *et al*, 1985) failed to detect any clinically significant effects of desglycinamide arginine vasopressin (DGAVP) in either alcoholic or Alzheimer-type dementia, and raised the possibility that the beneficial effect of vasopressin on performance was a non-specific stimulatory action that indirectly improved scores on memory tests. A later study by Peabody *et al* (1986*b*) found similar results using DDAVP (30–180 μg/day over three weeks). Such variability in outcome could be attributed to one of several factors, including the width of the 'therapeutic dose window', individual pharmacokinetic differences, variation in duration of therapy, and the inclusion of too many patients at a late stage of illness. As more potent, longer-acting vasopressin analogues become available, they too may be systematically evaluated, and most interest will focus on the effects of their chronic administration in patients with mild dementia.

ACTH

Although there are no reported abnormalities in the synthesis or release of adrenocorticotrophic hormone (ACTH) in dementia, there has been considerable interest in the treatment of cognitive disorders using ACTH analogues with the behavioural effects of ACTH but without its peripheral endocrine actions. This interest arises because of the stimulatory effects of ACTH on behaviour, recognised at least since 1955 (Quarton *et al*, 1955) but not distinguished from the hormonal actions of ACTH until synthetic analogues of ACTH fragments became available about 20 years ago (de Wied, 1969). The human psychopharmacology of ACTH peptides is now extensive (for reviews see Pigache & Rigter, 1981; Pigache, 1983). In summary, ACTH-like peptides may be involved in the acquisition of adaptive behaviour, and this involvement does not depend upon the ability of ACTH to release steroids since the same effects can be produced by ACTH $^{4-10}$, which is devoid of steroidogenic activity. Oral ACTH$^{4-9}$ with a glycine residue at position 10 (ORG 2766) has been most extensively studied in demented patients. Martin *et al* (1983) found ORG 2766 (40 mg daily *p.o.* for four weeks) had little effect in a double-blind cross-over placebo trial in 38 severely deteriorated female patients. Kragh-Sorensen *et al* (1986) found that ORG 2766 produced "clinically significant" effects in about 25% of 156 demented patients. Partanen *et al* (1986) examined both the symptomatic and EEG responses to ORG 2766 (40 mg daily *p.o.* for six months) or placebo. When the effects of other psychotropic drugs were taken into account, ORG 2766 did not prevent the deterioration in the EEG associated with the progress of AD. Analogues of ACTH are therefore without beneficial effects in AD.

Opiate antagonists

Although no abnormalities in central opioid systems have been detected in AD, several research groups have examined the effects of opiate receptor blockade

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in this disorder. This approach is based on the observation in healthy subjects that naloxone (1–10 mg i.v.) may improve some of the electrophysiological parameters associated with attention (Arnsten *et al*, 1983), although this is an inconsistent finding, especially at low doses. In a preliminary study in AD, Reisberg *et al* (1983) reported that low doses of intravenous naloxone produced clinical improvements. Later studies failed to reproduce these early findings (Steiger *et al*, 1985; Tariot *et al*, 1985). Longer-acting opiate antagonists do not appear to be more efficacious: naltrexone (Pomara *et al*, 1985; Hyman *et al*, 1985; Serby *et al*, 1986) and nalmafene (Weiss, 1987) were without significant clinical effect. The beneficial effects of opiate receptor blockade in dementia appear to be unpredictable; the study by Tariot *et al* (1986) suggests that the cognitive and behavioural actions of naloxone occur at about 5% of the dose required in younger, non-demented subjects. At present there is no indication for further studies on the endogenous opiate system in AD. However, opiate antagonists may prove to be of value in the treatment of dementia of presumed vascular origin. Naloxone can protect against the sequelae of cerebral ischaemia in some animal studies (e.g. Avery *et al*, 1983) and after acute stroke in clinical studies, especially when administered within the first 24 hours. In conjunction with the control of other risk factors for stroke, opiate antagonism may prove of value in the long-term treatment of cerebrovascular dementia when it is proposed that cognitive decline is caused by a succession of cerebral infarcts.

(g) Antiviral agents

Creutzfeld–Jakob disease (CJD) is a rapidly progressive dementia with an almost invariably fatal outcome (May, 1968; Manuelidis *et al*, 1978). Its features include abnormalities of muscular tone and movement, all attributable to a spongiform encephalopathy caused by an unconventional virus (Gajdusek, 1977). The infectious pathogen is believed to be similar to the infective agent in murine scrapie, which is often used as an animal model of transmissible dementia. Although antiviral drugs are without benefits in the animal model, in the absence of any other effective treatment these are thought justified in the terminal care of CJD patients. Initial single-case studies with idoxyridine were unsuccessful (Goldhammer *et al*, 1972; Herishanu, 1973) but several case reports of experience with amantidine are more encouraging (Braham, 1971; Sanders & Dunn, 1973; Sanders, 1979). The largest therapeutic trial reported to date included nine CJD patients in whom the diagnosis was confirmed at autopsy in seven subjects (Terzano *et al*, 1983). Four patients received amantadine (3.5–15 mg daily for an average of 32 days) and five others continued to receive supportive therapy. Although death appeared a little delayed in those receiving amantadine (seven months compared with three months for those on supportive therapy) this was not significant. The authors felt, however, there were some transient therapeutic benefits associated with amantadine (improved EEG, improved wakefulness, and reduced motor impairment) and they thought these effects might indicate some therapeutic potential, especially if amantidine were administered at an earlier stage. Other antiviral agents have been introduced late in the course of illness: interferon therapy was ineffective in two women with CJD (Kovanen *et al*, 1980) and acyclovir was likewise without effect (David *et al*, 1984; Newman, 1984). However, the course of illness in one patient with an histopathologically confirmed CJD diagnosis was repeatedly suppressed by vidarabine, which had little or no action in two other subjects (Furlow & Whitley 1982).

(h) Antihypertensive agents

Although AD is the commonest type of primary degenerative dementia, about one in eight dementias examined at autopsy have cerebrovascular disease without significant Alzheimer pathology (Jellinger, 1976; Katzman & Terry, 1983). Hypertension is associated, in most studies, with the development of cognitive impairment and, among the elderly, it is importantly linked with subsequent deterioration of cognitive performance (Scheinberg, 1988). However, the incidences of both hypertension and cognitive impairment increase with age and the association may be explained, at least in part, by chance. Further, it would not be surprising if hypertension, which is known to cause or exacerbate vascular disease, were to lead in turn to impaired cardiovascular performance, cerebrovascular accidents and, eventually, coarse brain disease and reduced mental efficiency. Although the majority of studies have detected an association in the absence of stroke between hypertension and impaired cognitive performance, the largest and most systematic to date found that among 2032 hypertensives neither blood pressure nor antihypertensive treatment was significantly associated with cognitive performance (Farmer *et al*, 1987).

It is clear from studies of the elderly that control of hypertension significantly reduces mortality and morbidity due to cardiovascular and cerebrovascular disease, but it is not yet established that the reduction of blood pressure in demented hypertensives contributes to improved life expectancy or is in fact desirable. One view, which was once widely held, is that the prognosis for all dementias is uniformly poor, their courses are unremittingly progressive and, on the assumption that the complex functions of dead or dying neurons cannot be restored, any attempt at treatment is doomed. Another view is that as cerebrovascular structures age, greater systemic blood pressure is required to maintain optimal cerebral perfusion (Strandgaard, 1976). If there were evidence to support this last hypothesis, then lowering of blood pressure in demented hypertensives would be contraindicated, as it would further compromise cognitive function.

Until recently, most clinical practice would have been based on the second view. Experience in the care of the demented elderly suggested that worsening of psychological and physical status was commonplace when hypertension was treated in demented patients. Such opinion, however, was based on experience with a wide range of antihypertensive agents, many of which are now known to exacerbate rather than relieve memory impairment and may have harmful effects on the autoregulation of cerebral blood flow. If it is assumed that the pathogenesis of vascular dementia involves progression from sustained hypertension to atherosclerotic cerebrovascular disease to a succession of cerebral infarcts to impaired cognitive performance, then the removal or control of factors predisposing to such a progression could possess distinct advantages for the hypertensive demented patient.

Meyer *et al* (1986, 1988*a*, 1988*b*) have completed the most extensive series of investigations on this topic. In summary, their studies have examined (a) the pathology of cerebral blood flow (CBF) during the course of vascular or Alzheimer-type dementias, (b) the relationship between cortical blood flow and reduced cognitive function in dementia, (c) incidence of 'risk factors', including hypertension, for stroke in multi-infarct dementia, (d) the question of whether hypertension should be treated in demented patients, and (e) the possibility that there is an optimum blood pressure (a 'therapeutic window') for demented hypertensives. They found a significant relationship between reduced cognitive test scores in multi-infarct dementia and mean local CBF (Kitagawa *et al*, 1984). This research group has provided data to support the contentions that while CBF is lower in both AD and vascular dementia, it decreases at least two years before the onset of vascular dementia but falls in step with the decline in cognitive function in AD (Rogers *et al*, 1986). They have also examined the effects of controlling blood pressure in two groups of hypertensive demented patients with presumed cerebrovascular dementia. In one group, blood pressure was reduced to within the upper normal range, and in the other group was reduced below this range. The findings were striking: improvements in cognitive function were clearly associated with the maintenance of systolic pressure within the upper normal range, but if systolic pressure was reduced below this range, patients showed a marked deterioration. This is the first study to examine systematically the effects of lowering blood pressure on cognitive function in dementia, and requires replication. It also raises important questions about the optimum choice of antihypertensive medication.

Non-demented, hypertensive old people were carefully investigated by Gurland *et al* (1988). Effective treatment of isolated systolic hypertension neither worsened nor improved cognitive function or behaviour. In this study, adequate control of blood pressure was achieved with diuretic alone (chlorthalidone) in 88% patients, and only a minority required alternative treatment (reserpine or metoprolol or hydralazine). The finding that lowering blood pressure in this group of non-demented subjects is probably safe is of potential relevance to the use of antihypertensives in multi-infarct dementia.

The Medical Research Council Working Party (1985) reported a trial of the treatment of mild hypertension, and raised the question of the optimum choice of antihypertensive agent for protection against strokes. If a succession of cerebral infarcts is presumed to be the essential component of vascular dementia, the results are pertinent here. The trial showed that bendrofluazide was almost three times as effective as propranolol in protecting against strokes and that this difference was even more marked between smokers. Previously, it had been assumed that most antihypertensives currently in use were equipotent in this respect, simply because of their ability to reduce blood pressure.

Centrally acting sympathetic blocking agents are associated with impairment of psychological functions when used to treat hypertension. In the demented elderly, these effects are not straightforward to interpret. In fact it would not have been surprising if Meyer *et al* (1986) had chosen to explain deterioration of some of their patients on the basis of the type of drug used rather than to implicate the final blood pressure. Antihypertensive treatment can have beneficial and harmful effects, capable of both slowing or reversing cognitive decline or producing new symptoms. In health, beta-blockers impair flicker fusion threshold, simple reaction time, and digit copying in some reports (McDevitt, 1985) but not others (Betts *et al*, 1985; Madden *et al*, 1986).

In hypertensives, memory impairment is linked to treatment with beta-blockers (Solomon *et al*, 1985) but not to angiotensin-converting enzyme (ACE) inhibitors (Lichter *et al*, 1986). Similarly, the ACE inhibitor captopril was associated with better performance at work and better 'life satisfaction' than either propranolol or methyldopa (Croog *et al*, 1986). In a study of adult hypertensives, nicardipine, a calcium channel antagonist, did not differ from propranolol (Callender *et al* 1986). Most studies of the cognitive effects of antihypertensives have linked methyldopa or the beta-blockers to cognitive impairment in treated hypertensives but the same does not appear to be true of the ACE inhibitors or the thiazide diuretics.

A potentially informative approach to the choice of antihypertensive drug is provided by studies on the effects of these drugs on CBF. Autoregulation of CBF is defined as the maintenance of a constant CBF in the face of normal changes in systemic blood pressure. In health, CBF is maintained by autoregulatory adjustment of resistance calibre during activities such as postural change, defaecation, etc. In both normotensive and hypertensive individuals the range of pressures within which autoregulation is effective may vary substantially. However, because cerebral flow is the same in both conditions, there must be increased cerebrovascular resistance in hypertension. Structural changes in the cerebral vasculature thus represent adaptations to sustained high blood pressure but have an important consequence for the hypertensive patient (Strandgaard *et al*, 1973). The chronically adapted resistance vessels are much less able to respond to hypotension, probably because their thickened vessels are less able to dilate than are healthy ones. The outcome for the demented hypertensive patient may well be catastrophic: if blood pressure is rapidly lowered then CBF will fall and ischaemic brain damage may ensue. Additionally, if the brain of the demented patient contains areas of normal tissue, which have retained their ability to autoregulate, these will maintain perfusion at the expense of adjacent damaged areas.

Patient studies support the view that ACE inhibitors have unique actions on CBF. For example, Britton *et al* (1985) showed that in ten patients with cerebrovascular disease, in spite of a fall of mean systemic blood pressure from 123 to 109 mmHg, the average CBF to an affected hemisphere tended to increase (by about 10%). In nine hypertensive control subjects receiving conventional antihypertensive therapies, mean systemic blood pressure fell from 118 to 114 mmHg, but CBF to an affected hemisphere tended to decrease (by about 11%). Unfortunately, the numbers of patients involved in this study were too few to have detected a statistically significant difference between groups given the size of the effect reported. Rajagopalan *et al* (1984) reported a similar result in a study of nine patients with severe congestive heart failure. After treatment with an ACE inhibitor (captopril) for between 4 and 15 days, mean diastolic blood pressure fell from 95 to 85 mmHg, while CBF increased significantly (from 61 to 74 units). Although it may be simplistic to equate CBF with cognitive performance (but see Meyer *et al*, 1988*a*), it is reasonable to take it into account when deciding upon the optimum hypotensive agent for a hypertensive demented patient.

Conclusion

There are no consistently effective drugs for the prevention of relief of dementia, but there is no lack of enterprise in the search for new treatments. This review has summarised how interest in neurochemical pathology has generalised from Parkinson's and Huntington's diseases to AD and on to other types of dementia, and how a better understanding of this pathology has led to novel therapeutic approaches.

The cholinergic hypothesis, which was the stimulus for much recent research activity, is no longer linked solely with Alzheimer's neuropathological changes, but is now confidently incorporated in several other hypotheses of memory dysfunction, whatever the associated neuropathology (e.g. the dementias associated with alcoholism (Lishman, 1986) and Parkinson's disease (Perry *et al*, 1985)). At the same time, initial emphasis on cholinergic deficits in AD has yielded to the more considered view that changes in non-cholinergic transmitter systems are also important in the pathogenesis of the cognitive and behavioural symptoms of AD, and may be amenable to therapeutic modification.

The problems of behavioural disturbances associated with dementia are worth intense research efforts, despite the fact that they have been relatively neglected. Community-based studies in this area may prove especially informative. More effective management of behavioural problems of demented patients in the community could substantially reduce the need for admission to a psychiatric hospital. The recognition that multiple transmitter deficits occur commonly in most types of dementia is now influencing the choice of treatment strategies to be evaluated in memory impairment and behavioural disturbances associated with organic brain disease. Proposals to modify simultaneously the function of several neurotransmitter systems are based on such observations.

The problems of ensuring that new drugs are indeed active at central sites putatively involved in the symptoms of dementia are important. Although most attention has been given to infusions of cellular preparations in the treatment of chronic neurodegenerative disorders, more conventional drugs have been administered by such direct routes. Harbaugh *et al* (1984) have demonstrated that it is practical to implant chronic intrathecal infusion devices in AD patients. Their use of the muscarinic agonist bethanechol yielded largely negative results, but similar techniques could prove crucial when used with other drugs. There may also be advantages to be gained from the use of agents in combination with already tested cholinomimetic drugs. Preliminary studies of combinations of physostigmine and phosphalidylcholine or piracetam have been largely negative (Growden *et al*, 1986), but other combinations may prove beneficial.

As knowledge has accumulated about the treatment of AD, so a fresh look has been taken at other dementias. Although it is probably naïve to equate cerebral blood flow and cognitive function, further studies of the potential benefits of controlling hypertension in patients with early features of cerebrovascular dementia should prove rewarding. Certainly, the results of Meyer *et al* (1986) require replication, and future studies of the treatment of hypertension in old people should include the detection of cognitive decline among the more usual measures of morbidity such as stroke or myocardial infarction.

Looking to the future, advances in understanding the pathogenesis of cerebrovascular disease will lead to novel therapies for dementias of vascular aetiology (following an argument already made, for example, on behalf of tissue plasminogen activator (Zivin *et al*, 1985)). Present knowledge, however, provides a substantial and sufficient basis for the investigation of many currently available treatments, and much could now be done to establish the value of controlling the harmful effects of acknowledged risk factors for multi-infarct dementia (Scheinberg, 1988). Studies on the memory impairments associated with Huntington's disease, alcoholism, and Parkinson's disease should benefit from experience of therapeutic efforts in AD. Specifically, the impetus given to dementia research by progress in AD is generalisable to other dementias. Creutzfeldt–Jakob disease, alcoholism, and brain injury have been discussed in this review, but Huntington's disease has been largely neglected. A literature search showed that almost without exception, treatment studies in Huntington's disease have examined only the abnormal movements, and a consensus did not exist concerning the exact nature and progress of the cognitive deficits in this condition. Selective neuronal loss is a characteristic feature of Huntington's disease, and one hypothesis attributes such loss to the toxic effects of neuroexcitatory amino acids, especially quinolinic acid (Schwarcz *et al*, 1982). Agents that specifically antagonise excitatory amino acids may provide a fertile source of novel drugs that prevent selective neuronal loss in AD and Huntington's disease (Schwarcz & Meldrum, 1985). Potentially, advances in understanding the molecular pathology of chronic neurodegenerative conditions may provide the most informative approach to the selection of such compounds. There is, therefore, certainly a strong case to be made for extending treatment paradigms to include new subgroups of dementia, among which alcoholic dementia will probably be the first.

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Winnicott: An Introduction

ADAM PHILLIPS

> "Health is much more difficult to deal with than disease."
> D. W. Winnicott

I

In a talk given in 1945 to the sixth form of St Paul's School, Donald Winnicott described his experience, as a schoolboy, of discovering Darwin's *Origin of Species*:

> "I could not leave off reading it. At the time I did not know why it was so important to me, but I see now that the main thing was that it showed that living things could be examined scientifically with the corollary that gaps in knowledge and understanding need not scare me. For me this idea meant a great lessening of tension and consequently a release of energy for work and play." (Quoted in Davis & Wallbridge, 1983, p. 24.)

Darwin had examined living things to explain their relation to each other. He realised that gaps in the evolutionary record were merely interruptions in the historical evidence for the continuity of species. Just as Freud would later describe the repressed histories of the individuals he treated, Darwin had reconstructed the invisible histories of species. Gaps in the evidence were openings, and both Darwin and Freud had been able to tell persuasive, apparently coherent stories about them. Winnicott implies by his remarks that he needed to be able not to close the gaps, but to find a way of examining them. They could be potential spaces for the imagination. He was to be preoccupied, as we shall see, by the idea of gaps, those 'spaces between' where there was room for the play of speculation.

In the master-plot of human development that he worked on for over 40 years, Winnicott tried to explain how the individual grows, through dependence, towards a personal way of being, how he becomes at once ordinary and distinctive according to the sense he has of himself, and how the early environment makes this possible. Growth was this ongoing task of psychosomatic integration. He was to stress the need for continuity of care – "good-enough mothering" – to sustain what he called the "going on being", the "life-line" of the infant, at the earliest stages of its life. He would talk, enigmatically for a psychoanalyst, of instinctual life as a possible "complication" in the individual's more fundamental needs for relationship. He would regard illness as the inhibition of that potential spontaneity that for him characterised the aliveness of a person. And he would come to think of psychopathology as originating from the breaks in continuity, the distractions in a person's early development: gaps caused by the intrusions and deprivations and natural catastrophes of childhood, most of which he saw as resulting from failures of parental provision. There were things the child had experienced but could not make satisfying sense of, and so find a place for in himself. For the infant who waits too long for his mother, for example, "the only real thing is the gap; that is to say, the death or the absence, or the amnesia" (Winnicott, 1971*a*, p. 26).

In Winnicott's view experience was traumatic for the child if it was incomprehensible, beyond the child's grasp. The onus was on the mother, at first, to present the world to the infant in manageable doses. And the onus on those helping mothers and infants, Winnicott believed, was to protect this process. "If it be true, or even possible," he writes, "that the mental health of every individual is founded by the mother in her living experience with her infant, doctors and nurses can make it their first duty not to interfere. Instead of trying to teach mothers how to do what in fact cannot be taught, paediatricians must come sooner or later to recognize a good mother when they see one and then make sure that she gets full opportunity to grow to her job" (Winnicott, 1958, p. 161).

Winnicott's work was devoted to the recognition and description of the good mother, and the use of the mother–infant relationship as the model of psychoanalytic treatment. And he often took for granted that what mothers did naturally, "what in fact cannot be taught", was a model for the skill of the psychoanalyst.

He examined, in particular, the paradox of traumatic experiences that were formative by virtue of their eluding the self, and the mother's role in facilitating in her infant a self available for

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personal experience. But Winnicott was to use the concept of the Self in an idiosyncratic and sometimes mystifying way that was not obviously compatible with traditional psychoanalytic theory. "A word like 'self' ", he writes, "naturally knows more than we do; it uses us and can command us" (Winnicott, 1965, p. 158). We will gather from the contexts in which he was used by this powerful word that he was asserting the presence of something essential about a person that was bound up with bodily aliveness, yet remained inarticulate and ultimately unknowable: perhaps like an embodied soul. "At the centre of each person", Winnicott (1965, p. 187) writes, "is an incommunicado element, and this is sacred and most worthy of preservation." This Self that he will describe as "permanently non-communicating" fits uneasily, of course, with the notion of psychoanalysis as primarily an interpretative practice.

The individual's Self was endangered, above all, Winnicott believed, by precocious adaptation to the environment. In *The Origin of Species* Darwin had noted what he called the "intermediate" or "transitional gradations" in the development of species, and the role of the environment in this process. He had realised the value, for survival, of individual diversity and variation, but also the need for the organism to comply with the demands of its environment. Organisms had to conform and adapt but also individuate prolifically in order to increase their chances of survival. Innovation and adaptation were mutually necessary, as those who were finally unable to adapt to their environment would not survive. In Winnicott's theory of human development it is the mother, as the first environment, who "actively adapts" to the needs of her infant. In Winnicott's terms the child has a natural right, initially, to use the mother ruthlessly for the recognition and gratification that his development requires. "Without someone specifically orientated to his needs," he writes, "the infant cannot find a working relation to external reality" (1984, p. 58). In time the mother will gradually limit her availability and so "disillusion" the child, and the child will become concerned about the consequences of his ruthlessness. But Winnicott, as we shall see, is committed to an idea of "natural" processes of development – derived from Darwinian biology – that the mother can adapt to and foster by her responsive attention. The word 'natural', as we shall also see, does a lot of devious work in Winnicott's writing. It could betray him sometimes – when he refers, for example, to "the part the woman plays in nature's comic opera" (Winnicott, 1964*b*, p. 110) – into a sentimentality that he was otherwise fiercely suspicious of.

The first relationship, in Winnicott's account, was one of reciprocity rather than overwhelming conflict or submission. But if the mother was unable, for reasons to do with her own development, to adapt to her infant's needs and was, herself, intrusively demanding, she would foster a precocious compliance in the child. To manage the demands of the mother, and to protect the True Self of personal need and preoccupation, the child would construct what Winnicott called a False Self. By introducing a language of reciprocity into the story of early human development Winnicott revised part of Darwin's account. He reverses the Darwinian equation by suggesting that human development was an often ruthless struggle against compliance with the environment. And this struggle was enacted in his writing where we find innovations in psychoanalytic theory and technique followed by explicit assertions of the continuity of his work with a more orthodox psychoanalytic tradition. We will see, in fact, a certain disingenuousness in the way Winnicott disguises his radical departures from Freud. "Mature adults", he wrote, "bring vitality to that which is ancient, old and orthodox, by recreating it after destroying it" (Winnicott, 1964*b*, p. 94). With blithe defiance Winnicott recreated, often beyond recognition, the work of everyone who influenced him.

Compliance was a crucial issue for Winnicott because of the fact of dependence. The infant relies on the mother's firm attentiveness for his survival. And the mother in turn depends upon the people around her that she needs. There is, as Winnicott once famously said, no such thing as a baby: "If you show me a baby you certainly show me also someone caring for a baby, or at least a pram with someone's eyes and ears glued to it. One sees a 'nursing couple' " (1964*a*, p. 88). Winnicott would derive everything in his work, including a theory of the origins of scientific objectivity and a revision of psychoanalysis, from this paradigm of the developing mother–infant relationship. He would elaborate what it was in the mother that the child depended upon, and this would lead him to questions that were rarely addressed in psychoanalytic theory: what do we depend on to make us feel alive, or real? Where does our sense come from, when we have it, that our lives are worth living? Winnicott approached these issues through the observation – one of his favourite words – of mothers and infants, and what became in time the "transitional space" between them. And he would be committed to linking these observations with insights derived from psychoanalysis. As the first paediatrician in England to train as a psychoanalyst, he was uniquely placed to compare his observations with the always reconstructed, retrospective histories of psychoanalytic treatment.

What went on between the mother and her infant was to be the source of Winnicott's most striking and characteristic insights. But it would be part of his incompatibility with Freud that these insights – the connection, for example, between infantile ruthlessness and adult sexuality – were rarely linked up by him with the place of the erotic in adult life. Fathers tend to turn up in his writing in brackets or parentheses. His most important theoretical contributions to psychoanalysis – transitional phenomena, primary creativity, ruthlessness, the antisocial tendency, the True and False Self – are never described in terms of the difference between the sexes.

Freud, though, had paid little attention in his work to the nursing couple or the details of infant care. He had invented a setting and treatment that were unwittingly reminiscent of early maternal care and he had also, of course, written of the dependent relationship recreated in psychoanalytic treatment. While he had acknowledged the significance, for later development, of the helplessness of the human infant and its precocious immaturity at birth, he had not given this helplessness the centrality it was later to assume for child analysts and the object-relations theorists who thought of themselves as continuing his work. It was the Oedipus complex – the three-person relationship – not the infant's early dependent vulnerability, that Freud saw as the crux of psychoanalysis. Though he worked out an essential pre-Oedipal schema of development, he put relatively little emphasis on the first relationship with the mother. And he tended to assume a certain developmental achievement in his patients that Winnicott would have questioned. From his case histories it seems that Freud believed his patients had more or less successfully negotiated the "long period" of helplessness and entered into the disappointing rigours of incestuous desire.

Freud was interested in the adult's struggle with incompatible and unacceptable desires which he saw as the transformed derivatives of the child's desire for his parents. This desire, that Freud referred to as infantile sexuality, was the precursor of and paradigm for adult sexuality. Out of a profound ambivalence, in Freud's view, the individual constructed an always precarious sexual identity, whereas for Winnicott, out of an always paradoxical involvement with others, the individual gathers the sense of a self he was born with as a potential. Where Freud was concerned with the individual's compromised possibilities for satisfaction, for Winnicott this is only part of a larger issue of the individual's possibilities for personal authenticity, what he will call "feeling real". In Winnicott's writing culture can facilitate growth, like the mother; for Freud it prohibits and frustrates, like the father. In Freud's view man is divided and driven, by the contradictions of his desire, into frustrating involvement with others. In Winnicott man can only find himself in relation with others, and in the independence gained through acknowledgement of dependence. For Freud, in short, man was the ambivalent animal; for Winnicott he would be the dependent animal, for whom development – the only 'given' of his existence – was the attempt to become "isolated without being insulated". Prior to sexuality as the unacceptable there was helplessness. Dependence was the first thing, before good and evil.

In the *Three Essays on Sexuality* (1905) Freud gives his account of the child's earliest developmental needs, the blueprint for all the competing psychoanalytic stories of human development that were to follow. In the first essay he makes a simple distinction that was to be important in the psychoanalysis of children. "Let us", he writes, "call the person from whom sexual attraction proceeds the sexual object and the act towards which the instinct tends the sexual aim." The first object of desire, Freud goes on to say, is for both sexes the mother. But the object, who is at first the mother, Freud claims is merely "soldered on" to the instinct. That is to say – and this is more obviously true of adult sexuality – there is for Freud no necessary connection between the instinct and its object, for which substitutes can easily be found. In this view the child's, and later the adult's, primary commitment is to the instinct and its satisfaction, not to a specific relationship. In fact, in Freud's view, the infant turns to the mother almost grudgingly out of the inability to be self-satisfied. In other words, dependence was imagined by Freud as a concession on the part of the infant. He comes, in a state verging on disappointment, to a belated awareness of the mother, who is literally an object to relieve the tension born of desire. The infant is conceived of as originally an omnipotent, exploitative hedonist (see Safouan, 1983).

With the advent of child analysis, and in particular with the work of Melanie Klein, the earliest stages of this object-relation with the mother came into focus in psychoanalysis for the first time. Instead of the discrete separation of subject and object, of the infant and its mother, the relational matrix became the object of attention. Different accounts of the child's emotional life began to emerge and more specific questions were asked about the place of the mother in the infant's world. Considering children's play as analogous to the free associations of adults, Klein applied her version of the classic psychoanalytic technique to the treatment of very young children. She interpreted their play and constructed unprecedented and revealing pictures of what she called the child's internal world. Stressing one aspect in particular of infantile sexuality, the infant's sadism, she was the first to formulate, though often in a dense psychoanalytic language of her own, the passionate intensity of early emotional life. As we shall see, her theories of primitive emotional development, and the significance of the child's destructiveness in the process, were to be crucial for Winnicott. His work, in fact, cannot be understood without reference to Klein. It is a continuous, and sometimes inexplicit, commentary on and critique of her work. The importance of the internal world and its objects, the elaborate and pervasive power of fantasy, the central notion of primitive greed – all these ideas Winnicott takes over from Klein and uses in his own way. As we shall see, they evolved different narratives of the developmental process and the mother's contribution to it. But her stringent theoretical positions, and the collusive devotion of her followers, provoked him without dispelling his own idiosyncratic approach.

Winnicott shared with Klein a fundamental belief in the decisive importance of the earliest stages of development. But from the very beginning, he claimed, the infant sought contact with a person, not simply instinctual gratification from an object. The infant starts life as a profoundly sociable being: he clamours for intimacy, not only for relief of tension – for relatedness, not simply for satisfaction. In fact satisfaction is only possible in a context of relatedness to the mother. "It is not instinctual satisfaction", he writes, "that makes a baby begin to be, to feel that life is real, to find life worth living" (Winnicott, 1971*a*, p. 116). It was maternal care, he believed, that made it possible for the infant self to be enriched, as opposed to overwhelmed, by instinctual experience. It was the mother's essential role to protect the self of her infant; instincts served the self, in Winnicott's view, they did not constitute it. It was "the self that must precede the self's use of instinct; the rider must ride the horse, not be run away with" (Winnicott, 1971*a*, p. 116). It was the "mother's job" to ensure that this happened.

Freud had said that the rider must guide the horse in the direction in which the horse wants to go. He was prescient in his sense that his insistence on the central and subversive importance of sexuality would threaten everyone's allegiance to psychoanalysis. Initiated by Klein, and reformulated by Winnicott, it was to be part of the contribution of what became known as the British school of object-relations theorists, to translate psychoanalysis from a theory of sexual desire into a theory of emotional nurture. It was as though the adult had been usurped by the infant. With the arrival of Melanie Klein in England in 1926, with the work of John Bowlby and Winnicott himself with children evacuated during the war, and with the insights derived from Anna Freud's version of child analysis, a new picture emerged in psychoanalysis of the significance of early relationships for the individual's development. Just as women were being encouraged to stay at home again after their crucial work during the war, coercive and convincing theories about the importance for children of continuous mothering, of the potential dangers of separation, began to be published which could easily be used to persuade them to stay there (see Riley, 1983). In British psychoanalysis after the war there was not so much a return to Freud, as there had been in France with the work of Lacan, as a return to Mother.

II

Under the aegis, though not the leadership, of Winnicott, a Middle Group emerged within the British Psychoanalytical Society. Strongly influenced by child analysis, but not exclusively allied with the work of either Klein or Anna Freud, these analysts – of whom Masud Khan, Charles Rycroft, Marion Milner, John Klauber and Peter Lomas are the most distinguished – formed no school or training of their own. Committed to pluralism rather than hero worship, their work coheres around a more eclectic developmental model. Coming, broadly speaking, from an empirical rather than a dialectical tradition, their work is characterised by an interest in observation and empathy, a suspicion of abstraction and dogmatism, and a belief in people's ability to make themselves known and be understood. Their theoretical papers refer continually to clinical work; there are few dazzling feats of interpretation or knowingness, and concern for the patient is expressed without irony. Imagination was a necessary term in their more or less shared conceptual vocabulary. Although obliquely influenced by existentialism, the Middle Group tended to draw their redescriptions of Freud from biology, ethology and literature rather than from linguistics and continental philosophy. Darwin, rather than Hegel or Nietzsche, was a presiding spirit in their work. There was no radical intent in their theory making. In their writings they did not make comprehensive theoretical assertions, nor was the tone one of shrewd enlightened dismay about the human condition.

For Winnicott, and those who were influenced by his work, psychoanalytic treatment was not exclusively interpretative, but first and foremost the provision of a congenial milieu, a "holding environment" analogous to maternal care. What Paul Ricoeur has called the "hermeneutic of suspicion" in Freud's work, is replaced by the attempt to establish an analytic setting in which the patient does not undergo authoritative translation – having his unconscious fed back to him, as it were – but is enabled by the analyst, as Winnicott wrote, "to reveal himself to himself". To begin with, the analyst is a certain kind of host: psychoanalysis, he wrote, "is not just a matter of interpreting the repressed unconscious [but] . . . the provision of a professional setting for trust, in which such work may take place" (Winnicott, 1987, p. 114–115). Interpretation, as part of the setting, aims to recognise and reconstruct what was absent in the parental provision, what early developmental needs were unacknowledged. The risk was that interpretation in analysis would be formative in a way that actually pre-empted the patient's own half-formed thoughts and feelings. Interpretation could be merely a way of hurrying – on the analyst's behalf – and analysis, like development, was, for Winnicott, about people taking their own time.

Cure, Winnicott wrote (1971*b*, p. 2), " at its root means care", care in the service of personal development. The therapist must have "a capacity . . . to contain the conflicts of the patient, that is to say to contain them and to wait for their resolution in the patient instead of anxiously looking round for a cure". Cure was not something that the therapist did to the patient. In his consultations with children Winnicott found that the significant moment was the one in which the patient surprised himself. In fact the development of a capacity to be surprised by oneself could be said to be one of the aims of Winnicottian analysis. A surprise, of course, eludes the expectations made possible by a body of theory. It is a release from compliance. From his case histories it is clear that Winnicott as an analyst was able to be convinced by his own surprises as well as the surprises of his patients (Winnicott, 1971*b*). Though psychoanalysts have written a lot about pleasure, Winnicott is one of the few that allows himself to be seen, in his writing, getting pleasure from what he does. And this, I think, is of a piece with one of his major contributions, which was to have evolved a genuinely collaborative model of psychoanalytic treatment in which the analyst creates a setting that also makes possible the patient's self-interpretations. Health for Winnicott was to do with the mutuality of relationship:

> "A sign of health in the mind is the ability of one individual to enter imaginatively and accurately into the thoughts and feelings and hopes and fears of another person; also to allow the other person to do the same to us . . . When we are face to face with a man, woman or child in our speciality, we are reduced to two human beings of equal status." (Winnicott, 1987, p. 117)

Interestingly, Winnicott's definition of health here echoes John Stuart Mill's definition of the imagination as the ability to "enter the mind and circumstance of another being". Though obviously prone to sentimental mystification, the idea of the reciprocity of the professional relationship was a new note in psychoanalysis, as were other of Winnicott's controversial and apparently whimsical pronouncements. When he wrote, for example, that "we are poor indeed if we are only sane" (Winnicott, 1958, p. 150), or that "true neurosis is not necessarily an illness . . . we should think of it as a tribute to the fact that life is difficult" (1958, pp. 318–319), or that "even when our patients do not get cured they are grateful to us for seeing them as they are" (1971*a*, p. 138), he was, in his own blithe and unbeglamoured way, radically revising conventional psychoanalytic pieties. A certain arch honesty, an often wilfully benign astuteness is part of Winnicott's distinctive style.

Although occasionally coy, his prose has none of the dreary earnestness or mystifying jargon that mars psychoanalytic writing after Freud and Ferenczi. His thought reflects, as André Green has written, "above all, a richly alive experiencing rather than an erudite schematizing". Because his papers were presented to a wide range of audiences, and because he was intent on being understood rather than copied, there is little arcane language in his writing. Instead there is a handful of idiosyncratic terms – holding, using, playing, feeling real, illusion and disillusion, true and false self, transitional phenomena – that, as we shall see, make up his developmental theory. What he refers to continually as the developmental process is the idol around which his work is organised. And the prominence of verbal nouns reflects his preoccupation with process rather than conclusion (he was, Masud Khan has written, "always mobile"). The notorious 'simplicity' of his language, however, is problematic. Though acutely aware himself of the way words are mobile – "they have etymological roots, they have a history: like human beings they have a struggle sometimes to establish and maintain identity" (Winnicott, 1987, p. 112) – he uses certain key terms as though they had no history in psychoanalytic thought. And while he recommends simple interpretations in analysis – "I never use long sentences unless I am very tired"(1965, p. 167) – his interventions in his case histories can be elaborate and surprisingly abstract.

The genre of simplicity in which Winnicott writes, a wry version of pastoral, is in fact a kind of elusiveness. But the shrewd ingenuousness of his writing, unprecedented in the psychoanalytic tradition, is consistent with one of his therapeutic aims: to protect the privacy of the self in the making of personal sense and, by the same token, personal nonsense. "In the relaxation that belongs to trust and to the acceptance of the professional reliability of the therapeutic setting . . . there is room for the idea of unrelated thought sequences which the analyst will do well to accept as such, not assuming the existence of a significant thread" (Winnicott, 1971*a*, p. 65). The need of the self to be both intelligible and hidden that he found in his patients is reflected in his style. There has never been a strong surrealist tradition in England but there has of course been a unique tradition of nonsense. And though Winnicott sounds like no one else writing in the psychoanalytic tradition, he can often sound curiously like Lewis Carroll. It is, in fact, part of his irreverence as a psychoanalyst to be entertaining. Only Winnicott (1971*a*, p. 108) could have written as a footnote to one of his most important papers: "When the analyst knows that the patient carries a revolver, then, it seems to me, this work cannot be done".

Though we can hear something of E. M. Forster, or his near contemporary Stevie Smith, in Winnicott's writing, there are no comparable echoes of previous psychoanalytic writers. He struggles to conceal the fact that he often writes uneasily in the psychoanalytic tradition, against the grain of its prevailing forms of seriousness and its fantasies of methodical rigour. His writing has its roots in the English romanticism of Wordsworth, Coleridge and Lamb (and has illuminating parallels, odd though it may seem, with the essays of Emerson and the work of William James). Much of his own work deviates from Freudian metapsychology, and unlike Klein and Anna Freud his work does not derive from specifically identifiable Freudian texts. As previous commentators have remarked: "Winnicott preserves tradition in a curious fashion, largely by distorting it . . . [with] his elusive mode of presentation and his absorption yet transformation of theoretical predecessors" (Greenberg & Mitchell, 1983, p. 189). By recontextualising crucial terms, he will gloss over their theoretical history. He will describe psychotherapy as a form of playing – "it has to do with two people playing together" (1971*a*, p. 44) – and at the same time express a marked preference for open-ended games in which play is not circumscribed by agreed-upon rules. In the Squiggle game, his most famous technical innovation, he invites a child to complete a rudimentary doodle that he does on a sheet of blank paper. By responding to the demand and turning the squiggle into something recognisable and shareable, the child offers a sample of his internal world. The repertoire of the child's possible responses is not circumscribed by the therapist. It cannot be calculated. In this reciprocal free association, this "game without rules", Winnicott saw the therapeutic potential of a traditional children's game, and adapted it to his psychoanalytic purposes. The charm and immediacy of his use of the technique described in his *Therapeutic Consultations in Child Psychiatry* could be as irresistible to the reader as it was to the child. It was Winnicott's vitality, his flair, that was unprecedented in psychoanalysis, and that created suspicion. By virtue of being new people, infants and young children can be difficult to understand. He could seem to embody a peculiarly modern but misleading ideal of perfect communication with children. There was something 'magical', his critics thought, in the fluency of his contact with the children he saw, as though all one could learn from his clinical accounts was that one was unable to be Winnicott. It will become clear that Winnicott had to be subtly pragmatic in his use of the psychoanalytic tradition. Sometimes he could allow himself to be idiosyncratic only by appearing to comply.

He was, however, explicit about his method of writing papers, which is, in the most interesting way, of a piece with his developmental theory. Introducing a radically innovatory paper to the British Psychoanalytical Society in 1945, he said:

> "I shall not first give an historical survey and show the development of my ideas from the theories of others, because my mind does not work that way. What happens is that I gather this and that, here and there, settle down to clinical experience, form my own theories, and then, last of all, interest myself to see where I stole what. Perhaps this is as good a method as any." (Winnicott, 1958, p. 145)

In the first sentence he refuses to comply with the way psychoanalytic papers are conventionally organised. He assumes influences are at work – "I gather this and that, here and there" – and he takes it for granted that in forming his own theories he will discover an indebtedness. He does not, it should be noted, refer to borrowing (on which subject psychoanalysis has always been silent) but to stealing. In his unique theory of delinquency, which he calls the antisocial tendency, Winnicott suggests, as we will see, that the child steals in symbolic form only what once belonged to him by right. The child is unwittingly trying to make up for a deprivation he experienced in the original commonwealth of his relationship with the mother, and he is alerting the environment to this fact. For Winnicott the antisocial act, like a regression in psychoanalytic treatment, is a return to the point at which the environment failed the child. He returns to find where what he hasn't got has come from, to the gaps in himself. Winnicott's method of writing papers, so recognisably close to ordinary experience, enacts this process.

As we trace the development of Winnicott's work we will find his evolving description of the mother–infant relationship mirrored by his own relationship with the psychoanalytic tradition. Like the infant's benign exploitation of the mother, which he describes, he will use the tradition according to his needs in the making of his own personal sense. He will suggest in one of his most remarkable late (1969) papers, "The use of an object and relating through identification" (Winnicott, 1971*a*, pp. 101–112), that the object only becomes real by being hated; the infant can only find the world around him substantial through his ultimately unsuccessful attempts to destroy it. Winnicott will test the resilience of the body of psychoanalytic knowledge in the development of his most recondite concept, the personal Self. Perhaps in becoming himself the psychoanalytic writer will, of necessity, have a delinquent relationship to the tradition, using it as he needs it. Winnicott, anyway, made it impossible for us to copy him: he is exemplary as a psychoanalyst, by being inimitable.

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Small Intestine Permeability in Schizophrenia

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Gastrointestinal permeability was assessed by means of absorption of ^{51}Cr-labelled EDTA in 24 patients with schizophrenia (12 in relapse and 12 in remission). The results were compared with those for patients with coeliac disease and those for normal controls. Significant differences between the schizophrenic patients and the normal controls were not established. The results for the schizophrenic patients in remission were no different from those for the patients in relapse, and there was no evidence from the study of an effect on gastrointestinal permeability of either anticholinergic or antidepressant medication. It is concluded that schizophrenia is, at least in the majority of cases, unrelated to coeliac disease.

The aetiological basis of schizophrenia remains unclear. Twin (Kallman, 1946; Slater & Cowie, 1971) and adoption (Heston, 1966; Kety *et al*, 1971; Rosenthal *et al*, 1971) studies have demonstrated the importance of genetic factors, but these alone do not explain the incomplete concordance between monozygotic twins (Crow, 1983). The search for significant aetiological factors continues, and the roles of diet and intestinal function have received some attention. Dohan (Dohan, 1970; Dohan, 1983; Dohan *et al*, 1984) has suggested that schizophrenia may have a shared genetic basis with gluten-sensitive enteropathy (coeliac disease) and that cereal grain components may act as the causal environmental agent for schizophrenia in those who are genetically susceptible.

The hypothesis that intestinal permeability (IP) in some schizophrenic patients is abnormal, and that this allows the passage of exorphins, giving rise to behavioural abnormalities, has been put forward by Wood *et al* (1987). That study demonstrated abnormal IP by cellobiose/mannitol absorption, in 33% of long-term patients, all orginally diagnosed as schizophrenic, but of whom only 17 out of 32 fulfilled St Louis (Feighner *et al*, 1972) criteria for schizophrenia. Each of the two groups showed the same proportion of patients with abnormal IP and only the need for anticholinergic medication distinguished the patients with abnormal permeability from those whose IP was in the normal range. It was suggested that the abnormal IP and consequent absorption of exorphins protected against Parkinsonian side-effects of phenothiazines. No normal control group was included in that study.

The availability of a safe, non-invasive, reliable and validated test of gastrointestinal permeability (Bjarnason *et al*, 1983) has enabled us to investigate IP in a group of 24 schizophrenic patients and to compare the results with those for a group of coeliac patients ($n = 19$) and a group of non-schizophrenic, non-coeliac controls ($n = 43$).

Method

The subjects of this study were 24 patients of Northwick Park Hospital in whom a clinical diagnosis of schizophrenia had been made and who at the time of the study were not detained under the Mental Health Act and were willing to participate in the investigation. The fulfilment of operational criteria for schizophrenia was not a criterion of entry for the study but the Present State Examination (Wing *et al*, 1974) was conducted in each case and the St Louis (Feighner *et al*, 1972) criteria for schizophrenia, which include chronic deterioration as an obligatory feature, were applied to the case-notes. The mental states of the patients at the time of the investigation were assessed using the standardised scale devised by Krawiecka *et al* (1977). Patients with morbid levels ($\geqslant 2$) of delusions, hallucinations or thought disorder were classed as being in relapse and those below those levels were classed as being in remission. Most patients were being prescribed neuroleptic drugs either orally or by depot injection and some were also receiving other psychotropic medication (Table I). It has been shown (Bjarnason *et al*, 1984*a*; Bjarnason *et al*, 1984*b*) that alcohol abuse and the use of non-steroidal anti-inflammatory drugs may increase IP. There were no patients who abused alcohol in the present study, and it is unlikely that any were ingesting alcohol at the time of the investigation. None of the patients was taking any non-steroidal anti-inflammatory drug. No patient was receiving or had received a gluten-free diet. All were Caucasian and ate standard Western diets. Details of the patients are shown in Table I.

The control group consisted of 43 normal volunteers (13 women) aged between 18 and 56 years. All were Caucasian and ate a standard Western diet. They had had no alcohol for at least one week and no non-steroidal anti-inflammatory agents for at least three weeks at the time of testing.

The method of assessing gastrointestinal permeability (Bjarnason *et al*, 1983) was as follows. A stock solution of ^{51}Cr-labelled EDTA (specific activity 1–2 mCi(mgCr),

TABLE I
Details of patients in relapse and in remission in terms of ages, diagnostic characterisation and drug treatment

Case no.	*Sex*	*Age*	*PSE categorisation*	*St Louis criteria for schizophrenia*	*Oral neuroleptics*	*Depot neuroleptics*	*Other psychotropics*
Patients in remission							
2	M	26^1:28	NS+	+ve		+;+	
4	M	23	DS+	+ve		+	
5	M	34^1:36	NS+	+ve		+;+	
6	M	21	HM+	−ve	+		
7	M	31	NS+	+ve		+	
8	M	55	DP?/AP?	−ve		+	
13	M	39	NS+	+ve	+	−	
17	M	33	NS+	+ve	+	−	Imipramine
19	F	38	NS	+ve	+	+	Procyclidine
22	F	48	NS+	+ve	−	+	Procyclidine, amitriptyline
23	M	44	MN+	−ve	+ (non-compliant)	−	Lithium, procyclidine
24	M	37	NS+	+ve	+	+	Procyclidine
Patients in relapse							
1	M	28	NS+	+ve	+	+	
3	F	31	NS+	+ve	+		
9	M	19	CS+	−ve	+		
10	M	35^1:37	NS+	+ve	+;0		
11	F	35	DS?	+ve			
12	M	29	NS+	+ve		+	
14	F	36	NS+	+ve	+	+	Procyclidine, imipramine
15	M	27	NS+	+ve	+	+	Procyclidine, temazepam
16	M	20	NS+	+ve	+		Imipramine
18	M	29	DP?/AP?	+ve	+(2 doses only)		Imipramine for 2 days only
20	F	20	NS PD	+ve	+	+	Imipramine, procyclidine
21	M	21	NS+	+ve	+		

1. Patient tested on two occasions.

Amersham International, Amersham, Bucks) was diluted in water so that each 10 ml had an activity of approximately 100 mCi (3.7 MBq). After fasting overnight, the subject drank 10 ml of ^{51}Cr EDTA solution, followed by 300 ml of water. After a further two hours, normal eating and drinking were resumed. Patients were encouraged to remain active and urine was collected over 24 hours. The estimated radiation dose received during the test is <0.1 mSv (effective dose equivalent), which is within the range for natural background radiation.

Deviations from the protocol

During the period of the investigation, three patients, who had already been included, presented on a second occasion. This provided us with the opportunity of retesting these individuals (cases 2, 5, 10, Table I), giving some assessment of the stability of the test and in case 10 allowing consideration to be made of the effect of neuroleptic drugs. In these cases mean values were used in the calculations.

Results

The percentages of the dose of ^{51}Cr EDTA excreted by the schizophrenic patients are shown in Table II.

Their mean percentage excretion was 2.17, s.d. 0.88 and that of the normal control group was 1.81, s.d. 0.60. Neither age nor sex of subject had any significant effect on percentage excretion. The samples showed a significant lack of homogeneity of variance ($P<0.03$) and for this reason the results in the groups were compared by the non-parametric test of Kruskal–Wallis. There was no significant difference in percentage excretion between the schizophrenic patients and the controls. This result is illustrated in Fig. 1, in which the percentage excretion of a group of untreated patients with coeliac

TABLE II
Urine excretion of ^{51}Cr EDTA (% dose) by schizophrenic patients

Patient number	*Cases in remission*	*Patient number*	*Cases in relapse*
2	2.66^1; 2.28 (2.47)	1	1.83
4	3.01	3	1.59
5	1.98^1; 0.93 (1.46)	9	1.28
6	1.98	10	2.36^1; 2.29 (2.33)
7	1.55	11	3.14
8	2.18	12	2.79
13	1.51	14	2.58
17	1.06	15	2.25
19	1.66	16	4.57
22	2.25	18	0.67
23	2.04	20	2.96
24	3.53	21	1.30
Mean	2.06±0.70		2.27±1

1. Cases tested on two occasions each two years apart. In these cases the mean value in parenthesis is used in the calculations.

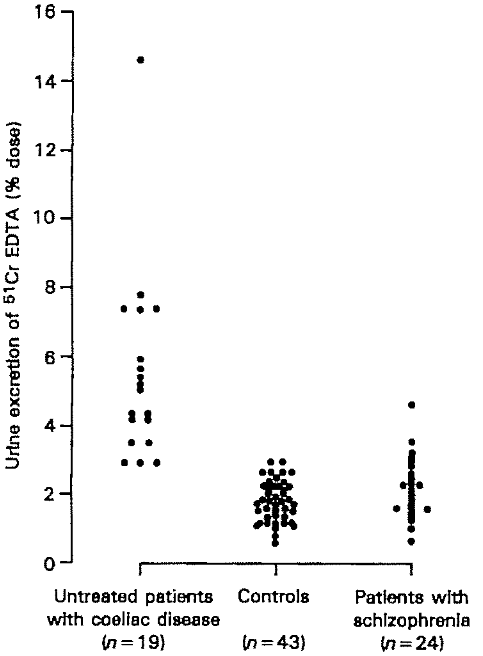

Fig. 1. Urinary excretion of ^{51}Cr EDTA (percentage dose). Each point represents the 24-hour urinary excretion of a single patient.

disease (mean 5.5, s.d. 2.7) who had been treated previously is also shown.

There were significant differences in percentage excretion between patients with coeliac disease and both normal controls ($P<0.001$) and schizophrenic patients ($P<0.001$). There was no difference in percentage excretion between schizophrenic patients in remission and those in relapse. From Table I, four cases did not fulfil the St Louis (Feighner *et al*, 1972) criteria for schizophrenia and two cases were placed in affective categories on PSE. Exclusion of these cases does not affect the overall results. Only one patient (case 10) was receiving no psychotropic medication when tested. This man had been tested two years previously when he was receiving neuroleptics, and the percentage excretion was very similar on the two occasions.

Discussion

Mean IP of the schizophrenic patients in this study did not differ from that of the control group. Patients with untreated coeliac disease, however, almost invariably showed increased IP.

There appeared to be no relationship between prescription of oral rather than depot neuroleptics and IP and by contrast with the findings of Wood *et al* (1987) there was no significant difference in IP between patients given anticholinergic medication (mean 2.47) and those who were not (mean 2.09). In the present study the trend was for higher IP in the procyclidine-treated group, whereas in the study by Wood *et al* (1987) the reverse was found. Also in the present study, as in that of Wood *et al* (1987), there was no difference in IP for patients treated with antidepressants (mean 2.34) compared with those who were not (mean 2.14).

Two of the patients in the present study (cases 16 and 24) showed percentage excretion levels (4.57 and 3.53) which were clearly above the normal range. These patients were male, relatively young, and had been ill for less than a year. Similar patients within this age group (e.g. cases 9 and 21) showed results well within the normal range.

Previous work which has investigated the possibility of gluten sensitivity in schizophrenic patients is inconclusive. Studies which have provided evidence for a relationship between psychiatric symptoms and gluten challenge or withdrawal (Dohan *et al*, 1969; Dohan & Grasberger, 1973; Singh & Kay, 1976; Rice *et al*, 1978) have not been supported by subsequent work (Potkin *et al*, 1981; Storms *et al*, 1982; Vlissides *et al*, 1986). It has been suggested that a subgroup of schizophrenic patients with borderline normal intelligence may be sensitive to gluten (Singh & Kay, 1976; Vlissides *et al*, 1986). The patients in the present study, including the two with the highest percentage of ^{51}Cr EDTA, were all of average intelligence.

Studies of food antibodies in psychiatric patients have similarly failed to reach a consensus. Dohan *et al* (1972) and Mascord *et al* (1978) reported raised titres of antibodies to gliadin in psychiatric patients compared with controls, but studies by McGuffin *et al* (1981), Kinnell *et al* (1982) and Rix *et al* (1985) failed to support this. Ashkenazi *et al* (1979) reported differences between psychotic patients, patients with coeliac disease and controls, in leucocyte migration inhibition in response to gluten fractions, but pointed out that the psychotic patients. in contrast to the coeliacs, showed no evidence of malabsorption or compromised nutritional status. Whether schizophrenia and coeliac disease occur together more frequently than chance might allow has yet to be demonstrated by adequate epidemiological investigations. An appropriate study would be of the case-control type (McMahon & Pugh, 1970). The available evidence argues against the hypothesis that sensitivity to gluten or its fractions is of relevance to psychiatric patients. The results of the present study suggest that schizophrenia, at least in the majority of cases, is unrelated to coeliac disease.

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Pre-morbid Psychopathology in Schizophrenia Spectrum

JOSEF PARNAS and AAGE JORGENSEN

In a prospective, longitudinal study of high-risk offspring of schizophrenic mothers, of several dimensions of pre-morbid behaviour 'peculiarity' predicted subsequent schizophrenia or schizotypy. Peculiarity/eccentricity may represent a subtle marker of the schizophrenic genotype. 'Pre-schizophrenics', as compared with 'pre-schizotypes', were characterised by affective dyscontrol, reflected in less introverted and more disturbed behaviour.

Both Kraepelin (1971, first published 1919) and Bleuler (1950, first published 1911) emphasised the similarity of pre-morbid characteristics in schizophrenia to mental deviations observed in relatives of schizophrenics, in schizophrenics in remission, and in very 'pure' or 'basic' forms of schizophrenia. Consequently, such characteristics could be regarded as 'trait' disorders or markers indicating presence of the schizophrenic genotype. In fact, in the current version of the DSM (DSM–III–R; American Psychiatric Association, 1987), there is a substantial overlap between schizotypal features and prodromal and residual symptoms of schizophrenia.

We have previously reported that elevated levels of defective emotional rapport and formal thought disorder at the age of 15 years predicted an adult schizophrenia spectrum in the offspring of schizophrenic mothers (Parnas *et al*, 1982*a*). Gunderson *et al* (1983) reported results from the Danish adoption sample indicating that eccentricity and paranoid traits were genetically related to typical process schizophrenia. Similar results emerged from a Norwegian twin study (Torgersen, 1985). Such results are consistent with the views of Bleuler and Kraepelin, who considered unique disturbances in interpersonal and social functioning as cardinal symptoms of schizophrenic disorders.

In the present study, we evaluated the prognostic value of different personal attributes as recorded pre-morbidly at the mean age of 15 years with respect to outcome ten years later. Specifically, we were interested in disentangling 'defective emotional rapport' into 'passive' (introverted) and 'inadequate' (peculiar) components. In fact, Stransky identified two dimensions in the Kraepelinian concept of 'emotional deterioration' (which according to Kraepelin was a fundamental symptom of schizophrenia): "First, the poverty or superficiality of emotional reactions; second, their incongruity with the ideational content dominating the psyche at that time, the latter being predominant at the onset of the disease" (Stransky, 1903).

Method

The present investigation is a part of an ongoing prospective longitudinal study of children of schizophrenic mothers (Mednick & Schulsinger, 1965). In 1962, 207 children (mean age 15 years) of schizophrenic women (of whom 91% meet the DSM–III–R criteria for schizophrenia (Jorgensen *et al*, 1987)) were pre-morbidly examined by a psychiatrist (Dr Fini Schulsinger) who completed an adjective check-list (ACL) consisting of 241 adjectives rated as appropriate or inappropriate to the subject and referring to the subject's mental status and behaviour during the interview.

In addition, a school behaviour questionnaire (SBQ) consisting of 30 questions was completed by the teacher most familiar with the subject. Behaviours were rated as present or absent. Since the study was prepared in the late 1950s, no modern reliability measures were performed.

In 1972–74, a ten-year diagnostic follow-up of 175 subjects of the original sample (mean age 25 years) was performed (Schulsinger, 1976) using a comprehensive interview consisting of the Present State Examination (Wing *et al*, 1974), Current and Past Psychopathology Scales (Endicott & Spitzer, 1972), and numerous additional ratings of various schizophrenia spectrum characteristics, such as subtle perceptual disturbances, formal thought disorder, and the quality of emotional rapport. On the basis of this reassessment, 15 subjects (including two deceased for whom only hospital record information was available) were diagnosed as ICD–8 schizophrenic (all of whom are DSM–III schizophrenic) and 29 subjects as ICD–8 borderline schizophrenics who fulfil the current DSM–III–R diagnosis of schizotypal personality disorder (Schulsinger & Parnas, 1988).

We have pooled schizophrenics and schizotypes ($n = 44$) on the assumption that they carried a greater genetic predisposition to disease, and on the basis that these disorders are of comparable inheritance (Inouye, 1970; Gottesman & Shields, 1972; Kety *et al*, 1978; Parnas *et al*, 1985). The remaining sample consisted of a group with various non-schizotypal diagnoses (diverse personality disorders and neuroses) ($n = 76$) and a group without any mental illness ($n = 55$). Pooling the diagnostic groups was determined not only by our theoretical assumptions, but also by our ultimate reliance on multivariate non-parametric statistics with binary outcome (Fleiss *et al*, 1986).

For the purpose of analyses, we have generated *a priori* scales from the ACL and SBQ. From the ACL it was

TABLE I
Pre-morbid behaviour scales

	Cronbach's α
Peculiarity[1]	0.68
peculiar *(ejendommelig)*, fatuous *(fjoget)*, awkward *(kejtet)*, clownish *(klovnet)*, giddy *(pjanket)*, queer *(sær)*, eccentric *(særpræget)*,	
Introversion–schizoid[1]	0.72
dreamy *(drømmende)*, cautious *(forsigtig)*, shy *(genert)*, inhibited *(hæmmet)*, introvert *(indadvendt)*, shut-in *(indesluttet)*, cool *(kølig)*, reserved *(reserveret)*, detached *(sky)*, silent *(tavs)*, withdrawn *(tilbageholdende)*	
Paranoid[1]	0.48
hostile *(fjendtlig)*, distrustful *(mistroisk)*, rigid *(rigid)*, formal *(stiv)*, guarded *(vagtsom)*	
Schizoid class behaviour	0.76
rarely asks questions, rarely takes the initiative, rarely takes part in spontaneous activities, seldom laughs or smiles, has difficulty in making friends, content with isolation, shy, reserved, and silent, uncomfortable in contact with classmates, uncomfortable in contact with the teacher, behaviour marked by passivity	
Class-disturbing behaviour	0.75
easily upset, excitement persists, disturbs class, dominating and aggressive, creates disciplinary problems	

1. Translations from the Danish.

possible to create scales measuring introversion/schizoid behaviour, peculiarity, and paranoid tendencies. In each case, a scale score was expressed as the number of adjectives appropriate to the subject. Similarly, from the SBQ we created scales measuring schizoid class behaviour (SCB) and class-disturbing behaviour (CDB).

The scales were subjected to an item analysis (Cronbach, 1951) which maximises biserial correlations between items and scale totals. The scales' composition and their measures of internal consistency appear in Table I. Cronbach's α could not be further improved by deletion of any items.

The composition of the scales was determined by the availability of items, our clinical judgement, and various literature sources. Since the nature of the data is at best ordinal, non-parametric statistical methods were employed (Mann–Whitney *U* test, Kendall's tau correlations). As a multivariate technique we have utilised logistic regression, which is adequate for ordinal data with dichotomous dependent variables (Fleiss *et al*, 1986). For the purpose of comparing relative contributions from schizophrenics and schizotypes to the possible differences, an analysis of variance with subsequent multiple range tests was employed. Probability levels below 5% were accepted as statistically significant.

Results

The comparison of schizophrenia spectrum (i.e. schizophrenia and schizotypy) v. the remainder of the high-risk sample on measures of pre-morbid behaviour is shown in Table II.

Those who later suffered schizophrenia spectrum disorders scored significantly higher on pre-morbid ratings of peculiarity and paranoia, whereas introversion, SCB, and CDB ratings did not discriminate between the groups.

TABLE II
Pre-morbid behaviour: schizophrenia spectrum v. others

	Peculiarity	*Introversion*	*Paranoid*	*Schizoid class behaviour*	*Class-disturbing behaviour*[1]
Schizophrenia spectrum ($n=44$)					
mean	1.18	2.59	0.82	7.68	4.27
s.d.	1.5	2.3	0.9	2.3	1.1
Other or no disorders ($n=131$)					
mean	0.51	2.35	0.53	8.01	4.39
s.d.	0.9	2.2	0.8	2.1	1.2
Two-tailed *P*, Mann–Whitney *U*-test	0.002	NS	0.03	NS	NS

1. High scale value corresponds to low level of abnormal behaviour.

TABLE III
Tau correlations within pre-morbid behaviour scales

	Introversion	*Paranoid*	*Schizoid class behaviour*[1]	*Class disturbing behaviour*[1]
Peculiarity	0.16**	0.36**	−0.08	−0.06
Introversion		0.32**	−0.13*	−0.11
Paranoid			−0.18**	−0.03
Schizoid class behaviour				0.17*
Class-disturbing behaviour				-

*$P<0.05$, 2-tailed, **$P<0.01$, 2-tailed.

[1] High scale value corresponds to low level of abnormal behaviour.

Because all five scales were correlated (see Table III), we performed a series of logistic regressions in order to separate correlated effects. Following free entry, only peculiarity retained its predictive power ($P=0.01$).

Since introversion, SCB and CDB were far from reaching predictive significance, we performed a separate logistic regression entering only peculiarity and paranoia and the interaction term between those two. Only peculiarity was a significant predictor ($P<0.001$).

In order to examine the specificity of the diagnostic differences, we performed a one-way analysis of variance on schizophrenia, schizotypy (schizophrenia spectrum), other diagnoses, and no mental illness. Peculiarity was a significant predictor of schizophrenia spectrum from the other diagnostic groups (i.e. other diagnoses and no mental illness), which did not differ from each other (mean values close to 0.5). In the case of paranoia, a similar analysis of variance indicated that those with no mental illness scored significantly lower than subjects in all other diagnostic groups, who did not differ from each other. These results are in agreement with those obtained from logistic regression analysis.

A comparison between predictors of schizophrenia v. schizotypal personality disorder appears in Table IV. 'Pre-schizophrenics' scored higher on CDB and lower on introversion. These were the only significant differences. Finally, we performed a logistic regression with free entry of all scales. Only high levels of CDB discriminated 'pre-schizophrenics' from 'pre-schizotypes' ($P<0.002$).

We did not detect any relationship between sex and the predictive value of the scales.

Discussion

The present investigation provides support for the original conceptualisations of which symptoms are cardinal to schizophrenia spectrum disorders. Both Bleuler and Kraepelin considered unique disturbances in emotional contact with the patient as so-called fundamental (or axial), i.e. pathognomonic, features of schizophrenia. This idea was shared by many of their contemporary researchers (Stransky, 1903, 1904; Jung, 1960, first published 1907; Kretschmer, 1925; Minkowski, 1927; Jaspers, 1963).

However, all these authors did not attribute the uniqueness of this emotional disturbance to pure introversion, but rather to a disorganisation of mental activity as a whole, e.g. "psychaesthetic disequilibrium" (Kretschmer, 1925), "loss of inner unity" (Kraepelin, 1971). Ruemke (1942) claimed that experienced psychiatrists may have, "often at a glance", a feeling that a person is schizophrenic. This "praecox feeling" signified the inability to empathise with the patient's personality as a whole.

TABLE IV
Pre-morbid behaviour: schizophrenic v. schizotypic

	Peculiarity	*Introversion*	*Paranoid*	*Schizoid class behaviour*[1]	*Class disturbing behaviour*[1]
Schizophrenic ($n=15$)					
mean	1.00	1.53	0.60	7.45	3.64
s.d.	1.4	1.7	0.9	2.8	1.6
Schizotypic ($n=29$)					
mean	1.28	3.14	0.93	7.78	4.54
s.d.	1.6	2.4	0.88	2.0	0.8
Two-tailed P, Mann–Whitney U-test	NS	0.03	NS	NS	0.04

[1] High scale value corresponds to low level of abnormal behaviour.

Jaspers (1963) formulated it similarly: "we do not grasp it; instead we enumerate a vast number of particulars or simply say un-understandable". Originally such an idea was vividly expressed by Stransky (1904) as a so-called "intrapsychic ataxia", i.e. the dissociation or dyscoordination between and within cognition, emotion and their expression (e.g. formal thought disorder, parathymia and paramimia). One may consider the dimension of peculiarity/eccentricity/oddity as related to the above-mentioned schizophrenic phenomena such as "loss of inner unity" and "intrapsychic ataxia", where components of expressive behaviour do not genuinely and cohesively fit with each other.

In our earlier study (Parnas *et al*, 1982*b*) we found pre-morbid measures of formal thought disorder predictive of later schizophrenia spectrum disorder. This finding is concordant with the general notion of Stransky and Bleuler that disintegration in schizophrenia is operating both within and between cognition and emotion. It may be appropriate to consider the so-called 'negative symptoms' as composite and multidetermined (Sommers, 1985). The symptom of inadequate rapport or eccentricity may actually represent a 'direct' reflection of the schizophrenic genotype, whereas other 'negative' symptoms, such as severe anergia, may constitute an interactional product of genetic vulnerability and organic insult to the central nervous system (Cannon *et al*, 1989; Parnas *et al*, 1988). In fact, recent factor analytic studies demonstrated that inappropriate affect (Gibbons *et al*, 1985) and bizarre behaviour (Bilder *et al*, 1985) do not correlate with avolition/apathy. Paranoid attitude, as observed pre-morbidly, was a univariate predictor of later schizophrenia spectrum, but was not specific to this diagnosis. Rather, it was the low scores of those with no mental illness that contributed to differences reported in Table II.

Our analyses did not reveal any predictive value of introversion or schizoid school behaviour with respect to later development of schizophrenia spectrum disorder. This indicates that introversion, as conventionally measured, is not specific to schizophrenic disorders. However, within the schizophrenia spectrum disorder, 'pre-schizophrenics' were more disturbed in school and less introverted than 'pre-schizotypes'. This finding suggests that 'pre-schizophrenics' as compared with 'pre-schizotypes' exhibit behavioural dyscontrol, possibly due to early environmental insults (e.g. perinatal damage (Parnas *et al*, 1982), or early emotional deprivation (Parnas *et al*, 1985)). It is, furthermore, noteworthy that SCB and CDB were slightly positively intercorrelated (Table III), indicating that these types of behaviour can coexist in the same individual. The results of this study are only preliminary, especially with respect to their specificity, because the study deals with a sample of young adults who may change their diagnosis in the future.

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Correlates of Positive and Negative Schizophrenic Syndromes in Nigerian Patients

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The two-syndrome concept of schizophrenia was investigated in a sample of 70 Nigerian schizophrenic patients. The positive and negative syndromes were studied in relation to demographic, historical, neurological and psychometric measures. The negative syndrome was associated with cognitive impairment, behavioural deterioration and left eye dominance, and also with poor pre-morbid educational achievement and longer length of current stay in hospital. The positive syndrome was unrelated to any of the independent variables. The two syndromes were not significantly related, supporting the view that they represent relatively independent dimensions of pathology. This provides further support for the validity of the Type I–Type II subtyping of schizophrenia in populations of patients from different cultural backgrounds, and suggests that the negative syndrome is related to the presence of neurodevelopmental deficits that possibly antedate the schizophrenic illness.

Ever since Kraepelin (1919) defined dementia praecox, the illness has always been regarded as heterogeneous in presentation and in outcome. The same belief informed Bleuler (1950) who, in coining the term 'schizophrenia', subtitled his book 'the group of schizophrenias'.

Most attempts to define a relatively narrow form of the illness that would follow a similar course and have identical prognosis for schizophrenic populations have met with little success. Thus, subdivisions into paranoid–non-paranoid (Tsuang & Winokur, 1974), schizoaffective–non-schizoaffective (Kasanin, 1933), and process-reactive (Stephens *et al*, 1966) have neither produced homogeneous groups in terms of prognosis nor led to the identification of biological correlates or aetiological factors.

One recent method of subtyping schizophrenia that has already proved useful in these respects is that proposed by Crow (1980). Crow postulates two schizophrenic syndromes, both of which reflect relatively independent dimensions of pathology but which can co-exist in a patient. Type I syndrome is characterised by 'positive' symptoms of hallucinations, delusions, and thought disorder. Type II syndrome is characterised by 'negative' symptoms of affective flattening and poverty of speech or muteness. Already, there is support for Crow's suggestions that the Type I syndrome is related to excess dopaminergic transmission (Crow *et al*, 1981), that the Type II syndrome is probably due to structural brain changes (Andreasen *et al*, 1982), that the Type II syndrome is less responsive to neuroleptic treatment than the Type I, and that the former may be associated with poor long-term outcome (Pfohl & Winokur, 1982). Negative symptoms have also been shown to bear some association with cortical neurological soft signs (Liddle, 1987) and left-handedness (Andreasen & Olsen, 1982).

With a few exceptions (Mathai & Gopinath, 1985; Kulhara *et al*, 1986), most of the studies relating to the negative and positive subtyping of schizophrenia have been conducted among populations of patients in industrialised countries. No study, to the present author's knowledge, has dealt with this issue among black African patients. Yet there is evidence that schizophrenia may follow a different course in industrialised countries from that followed in non-industrialised countries, even when an identical method of case selection has been used (World Health Organization, 1979). The possible roles of social and biological factors in bringing about this differential pattern of outcome have been speculated upon (Cooper & Sartorius, 1977). It has yet to be determined whether chronic patients from non-industrialised countries share identical clinical features with those from industrialised countries, and also what factors contribute to the emergence of features of deficit among them. More specifically, it is desirable to determine the validity of the Type I–Type II distinction between schizophrenic patients from various cultural backgrounds in order to test the universality of this concept. It is equally desirable to determine whether features that have been found to correlate with these subtypes of schizophrenia in previous studies bear an identical relationship among African patients.

Method

A study was made of 147 in-patients, unselected other than their being currently resident in the 9 wards of the Lantoro

Hospital, a long-term psychiatric care annexe of the Aro Neuropsychiatric Hospital, Abeokuta, Nigeria.

The mental state of the patients was assessed by use of the scale devised by Krawiecka *et al* (1977). For the present study, the scale was modified by rating flattening and incongruity of affect separately. A composite score of positive syndrome was devised from the scores for delusions, hallucinations, incoherence of speech and incongruity of affect while that of negative syndrome was generated from the scores for flattening of affect and poverty of speech or muteness (Owens & Johnstone, 1980).

The cognitive functioning of the patients was tested by administering the subtests of orientation, attention, and both forward and backward digit spans of the tests of the sensorium as described by Withers & Hinton (1971). The subtests were chosen because they could be given in Yoruba, the first language of the patients and the author. A battery of performance tests (adapted from Piran *et al*, 1982) was given to the patients to determine their motor and sensory lateralisation. For eye dominance, two tests were given: look through a keyhole, and point to the examiner's eye while closing one eye; for handedness, five tests were given: erase a pencil mark, throw a ball, touch a point on the wall, cut paper with scissors, and mix water with a spoon; for foot preference, three tests were given: kick a ball, step on a rubber bug, and touch a point on a wall. Objects needed for the tasks were presented in the midline in all cases. Writing was not employed for handedness because many of the patients were illiterate. A right eye/hand/foot preference was scored 0, while a left-side preference was scored 1. Total scores were computed for each of the subscales: 2 being most left-eyed, 5 most left-handed, and 3 most left-footed. Cortical neurological soft signs were assessed according to the procedure described by Quitkin *et al* (1976). The signs so assessed were: sensory inattention, right–left confusion, and finger-to-thumb mirror movements (right and left). A positive sign was scored 1 while negative or equivocal results were scored 0. A composite neurological soft sign score, termed a score of neurodysfunction, was obtained by summing the scores for separate tests. The patients were also evaluated for the presence and severity of involuntary movements, by the Abnormal Involuntary Movement Scale, AIMS (NIMH, 1976). Presence of involuntary movements was defined as a score of 2 (mild) on AIMS in any body area; severity of involuntary movements was defined as the sum of ratings of 2 and above in all body areas.

The current ward behaviour of the patients was rated by trained psychiatric nurses in charge of each ward. This was done by use of the scale devised by Wing (1961).

Only after completion of these assessments were the case notes of the patients analysed for demographic, clinical and historical details. The criteria of Feighner *et al* (1972) for schizophrenia were applied to the case notes. Of the 147 patients assessed, 70 fulfilled these criteria and formed the sample for the present paper. The following demographic and historical details were extracted from the case notes: sex, age, age at onset of illness, duration of illness, age at first admission to hospital, number of admissions, and duration of current admission. Details of treatment history obtained included cumulative length of neuroleptic exposure, current daily dosage of neuroleptics, and number of electroconvulsive treatments received. Neuroleptic doses were converted to their chlorpromazine equivalent according to the scheme described by Davis (1976). The level of previous education of the patients was rated according to the scheme: 0 – no formal education, 1 – primary education, 2 – secondary education, 3 – technical or advanced teacher training, 4 – polytechnic or university.

Results

The demographic, historical and treatment characteristics of the patients are listed in Table I. For 5 of the 70 patients, the information available in their case notes did not permit a reliable estimation to be made of their age during evaluation, age at onset of illness, age at first admission to hospital, or the duration of their illness. For an additional three patients, only the age at onset of illness could not be determined. Even though all the patients had been exposed to neuroleptic treatment, three were not receiving any such medication at the time of the study.

The male patients were similar to the females in all but two of the demographic and historical features: the males had a longer length of current stay in hospital, 101 months ± 121.8 v. 37.4 months ± 73.8 ($P<0.05$) and were receiving lower current daily doses of neuroleptics, 355.1 mg ± 356.6 v. 693 mg ± 998.3 ($P<0.05$). There were, however, no gender differences in the results of performance on the various clinical and neuropsychological ratings.

Table II shows the results of correlations of positive and negative schizophrenic syndromes with demographic, historical and treatment features. Only two features bore significant but modest relationships with negative syndrome: this syndrome correlated with a longer length of current stay in hospital and a lower level of previous education. No feature was significantly related to positive syndrome.

TABLE I
Demographic and historical characteristics of the patients (n = 70; 54 males, 16 females)

Variable	*Mean*	*s.d.*
Age:[1] years	39.1	11.8
Age at onset of illness:[2] years	25.3	6.7
Age at first admission to hospital:[1] years	29.1	8.8
Number of admissions	1.8	1.7
Duration of illness:[1] years	13.8	9.3
Length of current stay in hospital: months	86.9	115.4
Cumulative length of neuroleptic exposure: months	110	109.4
Number of ECTs	10.8	20.0
Current daily neuroleptic dose (CPZ-eq): mg	250[3]	(Range: 0–3800 mg)

1. Unknown in 5 patients.
2. Unknown in 8 patients.
3. Median dose given because the distribution is skewed.

TABLE II

Correlation between positive and negative symptoms and demographic and catamnestic variables

Demographic and catamnestic variables	*Syndromes (Krawiecka* et al *scale)* *Positive*	 *Negative*
Age	−0.23	0.13
Age at onset of illness	−0.14	−0.12
Duration of illness	−0.13	0.17
Number of admissions to hospital	0.04	−0.16
Length of current stay in hospital	−0.08	0.24*
Level of education	0.15	−0.25*
Number of ECTs	−0.07	0.20
Cumulative length of neuroleptic exposure	−0.04	0.12
Current daily dose of neuroleptic	−0.02	0.01

*$P<0.05$.

TABLE III

Correlations between positive and negative symptoms and neuropsychological measures

	Syndromes	
Neuropsychological measures	*Positive*	*Negative*
Cognitive test performance	−0.03	−0.41**
Current ward behaviour	0.20	0.55**
Presence of involuntary movements	−0.02	0.05
Severity of involuntary movements	−0.12	0.04
Neurodysfunction	0.09	−0.04
Eye dominance	−0.09	0.32*
Foot preference	−0.02	−0.04
Handedness	−0.04	−0.04

*$P<0.01$.
**$P<0.001$.

Similarly, positive syndrome was unrelated to any of the evaluated neuropsychological features (Table III). However, negative syndrome was highly related to poor cognitive test performance, behavioural deterioration as assessed on the wards, and left eye dominance. The presence of tardive dyskinesia or its severity, the composite sum of elicited cortical neurological soft signs, handedness, and foot preference were all unrelated to negative syndrome.

The relationship between positive and negative syndromes was then examined. The correlation between the two was not significantly different from zero (Pearson's $r=-0.05$).

Discussion

The validity of the concept of Type I and Type II schizophrenia as proposed by Crow (1980, 1985) was investigated in a sample of Nigerian long-term schizophrenic in-patients. A battery of neuropsychological assessments was administered to the patients, blind to their diagnosis. Their scores on the rating of negative and positive syndromes were then correlated with their demographic, historical and neuropsychological attributes. The results of the correlational analyses showed that negative syndrome bore significant associations with various historical and assessed variables while positive syndrome showed no such relationship.

In consonance with the observations of a number of other authors (Owens & Johnstone, 1980; Johnstone *et al*, 1981; Mathai & Gopinath, 1985), the present study found a strong association between negative syndrome and both cognitive impairment and behavioural deterioration. This observation supports the view of Crow (1980, 1985) that these features constitute the 'deficit state' or Type II schizophrenia syndrome. The finding in the present study of a strong association between negative syndrome and left eye dominance probably reflects Crow's view that the Type II syndrome is associated with structural brain changes. Andreasen & Olsen (1982) found a higher prevalence of left-handedness in schizophrenics with negative symptoms than in those without. The present study found no association between negative syndrome and either handedness or foot preference. This inconsistency might reflect the observation that cultural pressures play an important role in the manifest lateral motor preferences of Nigerians (Payne, 1987). The significance of the present finding relates to the observation that birth stress is related to eye rather than hand or foot preference (Nachshon & Denno, 1987).

The suggestion that involuntary movements may be a component of the deficit state or Type II syndrome (Crow, 1985) was not supported by the present study. No association was found between negative syndrome and either the presence or the severity of these movements. Studies that have found such a relationship have been conducted among elderly schizophrenic patients (Owens *et al*, 1985; Waddington *et al*, 1987). Such an association has generally not been found among young schizophrenics (Opler *et al*, 1984; Kolakowska *et al*, 1986). The sample of patients for the present study was composed of patients who were mostly in their fourth decade. It seems probable, therefore, that structural brain pathology, which is said to underly the Type II syndrome, is related to involuntary movements in elderly but not in young schizophrenics.

There was a modest relationship between negative syndrome and length of current stay in hospital. This observation is similar to that of Owens & Johnstone

(1980). Compared with the degree of association between negative syndrome and some assessed neuropsychological measures, this finding does not provide much support for the notion that institutionalisation could explain the occurrence or severity of negative symptoms. It seems more likely that negative symptoms reflect an underlying pathological process in a subgroup of schizophrenic patients, and that the presence of these symptoms leads to a prolonged stay in hospital.

Negative syndrome also showed a modest correlation with poor pre-morbid educational achievement. A number of investigations have made a similar observation (Andreasen & Olsen, 1982; Pogue-Geile & Harrow, 1984). As suggested by Pogue-Geile & Harrow (1984), this association may reflect either poor early functioning due to underlying processes leading to the later development of negative symptoms in those who become schizophrenic, or the interaction between early deficits and schizophrenia leading to negative syndrome. Taken together with the observation of an association between this syndrome and left eye dominance, it seems plausible to suggest that negative syndrome is associated with neurodevelopmental deficits that antedate the onset of the schizophrenic illness.

The result of the present study does not support the notion that positive and negative syndromes "are at opposite ends of a continuum" (Andreasen & Olsen, 1982). Rather, as suggested by Crow (1985), they appeared to be independent "dimensions of pathology". Some of the inconsistencies that emerge in studies in this area may possibly be explained by differences in the definition of what constitute negative symptoms. Crow (1985) has emphasised the need for these symptoms to be defined narrowly (e.g. by the use of the Krawiecka scale).

This study confirms the validity of the concept of Type I–Type II subtypes of schizophrenia among black African patients. It shows that factors previously identified as associated with the 'deficit state' in schizophrenic patients in industrialised societies have identical significance for patients from non-industrialised countries.

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Patterns of Psychotropic Drug Use in a Spanish Rural Community

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Psychotropic drug use was investigated using a two-stage survey of a random sample of persons aged 17 and over from a rural Spanish community. It was found that 6.9%, 11.8% and 25.1% of the population were consuming psychotropic, analgesic and somatic medicines respectively. Women presented a higher rate of psychotropic use than men (prevalence for women 10.7%, for men 2.6%). This female predominance was found to be significantly related to sociodemographic and medical factors. Psychotropic use was also associated with the physical health of the respondent. The coexistence of physical and mental illness generated an increase of consumption, whereas the absence of both types of illness was associated with a very low rate. The rates for physical and for mental illness alone were intermediate and were almost equal.

Since the introduction of tranquillisers, psychotropic drugs are being used increasingly in medical practice and also in the general population (Williams, 1980), and such drugs currently account for about 15% of all prescriptions dispensed at retail pharmacies. This situation has heightened interest in the study of factors that might influence the rates and patterns of use of such drugs.

Until now, the aim of most studies in this area has been to investigate, in general-practice settings, the proportion of patients receiving a prescription for psychotropic drugs (e.g. Skegg *et al*, 1977; Harris *et al*, 1977; Grimsson *et al*, 1979). The prescription rates reported vary between 9.4% (Harris *et al*, 1977) and 15.5% (Skegg *et al*, 1977). Related studies based on prescriptions dispensed at retail pharmacies have yielded similar results (Williams, 1980; Marks, 1983). Studies such as those just mentioned, however, should be interpreted with caution as they offer only a rough estimate of the quantity of drugs consumed. It is thus preferable to consider studies which provide information about prevalence of consumption in the general population. Many such studies are American (e.g. Mellinger *et al*, 1971; Uhlenhuth *et al*, 1978; Craig & Van Natta, 1978). The prevalence figures reported vary widely, from 11.9% (Craig & Van Natta, 1978) to 39.6% (Mellinger *et al*, 1971). These variations are mainly accounted for by methodological differences. British community studies on drug consumption, which are characterised by the use of a stricter and more homogeneous methodology, show lower rates of consumption, with less variation – between 10% and 12% (Murray *et al*, 1981). Less information is available, however, from other European countries, including Spain (Tognoni *et al*, 1981; Cooperstock & Parnell, 1982). In fact the only Spanish data on psychotropic drug consumption comes from a cross-national survey conducted by Balter *et al* (1974). In this survey the Spanish sample presented the lowest reported prevalence of drug consumption (males 7.0%, females 12.5%, all persons 9.75%).

Sociodemographic factors appear to be associated with psychotropic drug use. Most studies have found drug consumption to be higher for women than for men, and to increase with increasing age (e.g. Skegg *et al*, 1977; Cooperstock, 1978; Williams, 1979; Murray *et al*, 1981; Cooperstock & Parnell, 1982). The relationships with other factors such as marital status, social class, educational level and occupation are, however, less clear, although some authors suggest that psychotropic drug use is associated with life situations characterised by the lack of social support (Gabe & Thorogood, 1986; Cafferata *et al*, 1986). A relationship has also been found between psychotropic drug use and high scores on psychopathological instruments such as the General Health Questionnaire (Murray *et al*, 1981), the CES–D Depression Scale (Craig & Van Natta, 1978), and versions of the Hopkins Symptom Check List (Uhlenhuth *et al*, 1978; Mellinger *et al*, 1978). Psychotropic drugs have also been widely used as adjunctive therapy for physical conditions (reviewed by Williams, 1978).

This paper deals with the use of psychotropic drugs in the general population. Using data from the Community Mental Health Survey of Cantabria (Spain) (Vázquez-Barquero *et al*, 1986, 1987*a*,*b*), we consider (a) the extent and pattern of use of psychotherapeutic drugs, and (b) the way in which sociodemographic, psychopathological and medical factors interact with psychotropic drug consumption.

Method

The aims and design of the Community Mental Survey of Cantabria (Spain) are described in previous papers (Vázquez-Barquero *et al*, 1987*a*). The survey was conducted in a rural area located on the eastern side of the bay of Santander. The area has a population of about 9252, and extends for approximately 105 km^2. It comprises several small villages surrounded by a large number of isolated farms where most of the family land lies around the house. Life on the farms is centred on dairy farming. In the coastal parts of the area there are complementary activities related to summer tourism and fishing. In the villages it is possible to detect a progressive process of urbanisation and industrialisation based on light industry and the development of public and community services. This community was chosen to represent from a sociodemographic and structural point of view the non-urban coastal part of the region of Cantabria. In this sense it could be seen as representative of the way of life in the rural coastal areas of northern Spain.

Sampling

Details of the method by which respondents were sampled are given by Vázquez-Barquero *et al* (1987*a*). In brief, the design involved two-stage sampling. In the first stage a random sample of 1223 persons, stratified by sex and age, was drawn from the electoral register; thus it was made up of persons aged 17 years and over. First-stage respondents were asked to complete the 60-item General Health Questionnaire (GHQ; Goldberg & Williams, 1988) in its Spanish version (Vázquez-Barquero *et al*, 1986), and a variety of other social and health questionnaires. The criteria of inclusion in the second-stage sample were as follows: (a) all persons who scored 12 or more on the GHQ–60 in the first stage; and (b) an approximately equal number of persons who scored below 12 on the GHQ in the first stage; these were selected at random from two batches of below-threshold scorers (0–5 and 6–12 scorers). The description in numerical terms of this sampling design is shown in Table I.

TABLE I
Distribution of GHQ scores at the two stages by sex

GHQ score	*First-stage sample*			*Second-stage sample*		
	Males	*Females*	*Total*	*Males*	*Females*	*Total*
<12	68	159	227	68	151	219
6–11	85	136	221	16	31	47
0–5	428	347	775	93	93	186
Total	581	642	1223	177	275	452

Sample evaluation

Detailed descriptions of the method of evaluating respondents in the two stages of the survey are given elsewhere (Vázquez-Barquero *et al*, 1986, 1987*a*). For the purpose of the present investigation, the evaluation can be considered in terms of physical and mental health.

Evaluation of physical health and drug use

The assessment of physical health was described by Vázquez-Barquero *et al* (1988). Basically, physical illness was considered to be present when a person presented evidence of being, at the time of the survey, under medical care because of a somatic illness of a non-transient nature. The health questionnaire included questions directed to ascertain whether respondents were 'currently' and on a 'regular basis' taking medicines of any sort, even analgesics, sleeping pills or nerve pills. The period surveyed was restricted to the preceding two weeks. If applicable, respondents were asked to provide evidence of consumption by showing the doctor's treatment order or the medicine bottle. Additional data were recorded about the source of the drug and about patient opinion of the reasons for consumption. For the purpose of this study drugs have been classified in the three main groups of (a) 'somatic', (b) 'analgesics', and (c) 'psychotropic'. Psychotropic was defined to include neuroleptic antipsychotics, anxiolytics, non-barbiturate hypnotics, barbiturates, tricyclic antidepressants, MAO-inhibitors, stimulants, and other psychotropic drugs including lithium. As it was found in the preliminary analysis that there was no consumption of certain psychotropic drugs – barbiturates, stimulants, MAO-inhibitors, and lithium – these categories were abandoned. In addition, as the figures for neuroleptic antipsychotics were negligible, these drugs were incorporated together with the anxiolytics into a category of 'tranquillisers'. Thus finally the three categories of 'tranquillisers' (mainly benzodiazepines), 'hypnotics' (mainly benzodiazepines used as night sedation), and 'antidepressants' (mainly tricyclic antidepressants) were considered.

Evaluation of mental health

The mental health status of respondents was assessed in two independent ways. For a detailed description see Vázquez-Barquero *et al* (1987*a*). The two methods were by the General Health Questionnaire and by the Present State Examination.

Evaluation by General Health Questionnaire. As mentioned, the GHQ–60 in its Spanish version was used to assess the mental health of first-stage respondents. All persons in the sample were visited at home by suitably trained interviewers. During a single session they were asked to complete, in addition to the GHQ-60, a medical questionnaire and a social questionnaire. The GHQ scoring method was used, with a cut-off score of 11 (Goldberg & Williams, 1988). Schedules were divided into four different batches in terms of GHQ score, giving a breakdown of the population into 0–5, 6–11, 12–19, and 20+ scorers. The GHQ score was used as the criterion for the selection of subjects to be included at the second stage (Vázquez-Barquero *et al*, 1987*a*). It was also used in a different analysis, as in this paper, as an indicator of mental disturbance. The validity figures reached in this survey by the GHQ when compared with the PSE are given elsewhere (Vázquez-Barquero *et al*, 1986).

Evaluation by Present State Examination. All subjects included in the second stage were interviewed, at their homes, by psychiatrists using the ninth 140-item version of the Present State Examination (PSE; Wing *et al*, 1974). PSE data were analysed using the CATEGO program and the Index of Definition (ID; Wing *et al*, 1974; Wing & Sturt, 1978). The ID allows eight degrees of definition of symptomatology to be established; at the threshold and definite levels (5–8), disorders are sufficiently well defined to be considered pathological. Subjects also received a CATEGO diagnosis. PSE data were used as the final indicator of the psychiatric morbidity for the community. However, because of the stratified sampling in the second stage, each of the prevalence figures has to be weighted in order to reconstitute the original sample (Vázquez-Barquero *et al*, 1987*a*).

Definition of social variables

The nature and characteristics of the social categories used are described in a previous paper (Vázquez-Barquero *et al*, 1987*a*). Social status was defined according to occupation, except when the respondent was working on the family farm, in which case it was established by taking into account the extent and characteristics of the property. The social status of women was decided according to their own occupation for women working full-time outside the house; in other cases the social status of the head of the household, whether husband or father, was taken. In view of the sociological characteristics of the community under study, this categorisation of social status should not be taken as the equivalent of the traditional urban social class concept.

The six original educational levels have been combined into two final categories: 'higher', which includes from university studies to secondary education, and 'lower', covering primary education and the illiterate. By 'absence of work' we mean the lack of any paid working activity, whether because of unemployment, retirement, or for medical reasons; this category was also expanded, in the case of women, so as to include those who worked exclusively as 'housewives'.

Statistical analysis

For the analysis of data we applied the χ^2 test (corrected for continuity) (Siegel, 1978), except where ordinal data had to be analysed (Table VIII), in which case we used the Kolmogornov–Smirnov test, following the indications of Siegel (1978).

Results

Details of the characteristics of the respondents, and an analysis of the extent and correlates of psychiatric morbidity, have been presented elsewhere (Vázquez-Barquero *et al*, 1986, 1987*a*,*b*, 1988), so they will not be considered here.

Prevalence of psychotropic drug use

The proportions of men and women using the different types of drug (psychotropic, analgesic, somatic) at the time of the survey are shown in Table II. In all, 307 (25.1%) subjects reported that they had taken somatic medicines, 143 (11.8%) reported that they had taken analgesics and 84 (6.9%) that they had taken psychotropic drugs. The prevalence of consumption of psychotropic drugs is 10.7% for females and 2.6% for males. For each type of drug, the rate of consumption is significantly higher for women than for men (psychotropic, $\chi^2=30.5$, d.f. $=1$, $P<0.001$; analgesic, $\chi^2=27.5$, d.f. $=1$, $P<0.001$; somatic, $\chi^2=5.2$, d.f. $=1$, $P<0.05$). Among subjects taking psychotropic drugs a considerable proportion are taking them in association with analgesic or somatic medicines (males, 40%; females, 70%). This association is significantly higher in women than in men ($\chi^2=4.4$, d.f. $=1$, $P<0.05$). The female predominance in psychotropic drug use tends to disappear in the group taking psychotropic drugs only and is enhanced in the group taking these drugs in association with other medicines.

Psychotropic use and sociodemographic factors

The proportion of psychotropic drug users in each age group is shown in Table III. In both sexes, increasing age is associated with a higher likelihood of using psychotropic drugs (total psychotropic consumption: males ≤ 54 years v. males ≥ 55 years, $\chi^2=4.4$, d.f. $=1$, $P<0.05$; females ≤ 34 years v. females ≥ 35 years, $\chi^2=15.8$, d.f. $=1$, $P<0.001$). Table IV shows that the age relationship for tranquillisers and hypnotic drugs differs from that for antidepressants: the proportion of subjects taking tranquillisers and hypnotics increases significantly with age, whereas this does not happen with antidepressants (tranquillisers, ≤ 34 years v. ≥ 35 years, $\chi^2=16.7$, d.f. $=1$, $P<0.001$; hypnotics, ≤ 34 years v. ≥ 35 years, $\chi^2=8.4$, d.f. $=1$, $P<0.01$; antidepressants, ≤ 34 years v. ≥ 35 years, $\chi^2=0.32$, d.f. $=1$, NS).

Whereas for males marital status was not significantly related to psychotropic drug consumption, there was significantly higher consumption in married women (percentage of psychotropic drug consumption: male single 3.9%, male married 2.0%, $\chi^2=0.9$, d.f. $=1$, NS; female single 5.2%, female married 15.4%, $\chi^2=3.9$, d.f. $=1$, $P<0.05$). The interaction between marital status and age was not tested because of the low sample figures.

The relationship between sociological factors and psychotropic drug consumption is shown in Table V. We found that the lower educational level was significantly associated in females with psychotropic drug use ($\chi^2=13.7$, d.f. $=1$, $P<0.001$). In males, although there was a tendency in the same direction, the difference was not significant ($\chi^2=3.7$, d.f. $=1$, NS). Absence of work

TABLE II

Prevalence of consumption of psychotropic and other drugs

Type of drug	*Males* (n = *581*)		*Females* (n = *642*)	
	Number	*%*	*Number*	*%*
Total psychotropic	15	2.6	69	10.7
Psychotropic only	9	1.0	21	3.3
Psychotropic associated with other medicines	6	1.1	48	7.5
Total analgesic	38	6.5	105	16.4
Total somatic	128	22.0	179	27.7

TABLE III

Psychotropic drug use by sex and age

Sex and age[1]		*Total psychotropic use*	
		Number	*Prevalence (%)*
Males <34	(n = 179)	2	1.1
Males 35–54	(n = 185)	3	1.6
Males >55	(n = 217)	10	4.6
Females <34	(n = 182)	5	2.7
Females 35–54	(n = 225)	27	12.0
Females >55	(n = 235)	37	15.7

1. n is number in first-stage sample.

TABLE IV

Consumption of tranquillisers, antidepressants and hypnotics (considered separately[1]*) by age*

Age[2]		*Tranquillisers*		*Hypnotics*		*Antidepressants*	
		Number	*%*	*Number*	*%*	*Number*	*%*
<34	(n = 361)	5	1.4	—	—	4	1.1
35–54	(n = 410)	27	6.6	6	1.5	6	1.5
>55	(n = 452)	38	8.4	17	3.8	6	1.3
Total	(n = 1223)	70	5.7	23	1.9	16	1.3

1. Numbers do not add up to 94 because there are overlapping groups of consumers.
2. n is number in first-stage sample.

TABLE V

Psychotropic drug use by sex and sociological factors

Sociological characteristics	*Males*			*Females*		
	Number in first-stage sample	*Taking psychotropic drugs*		*Number in first stage sample*	*Taking psychotropic drugs*	
		Number	*%*		*Number*	*%*
Social status						
Higher	306	7	2.3	268	28	10.4
Lower	275	8	2.9	374	41	11.0
Educational level						
Higher	142	0	0.0	133	2	1.5
Lower	439	15	3.4	509	67	13.3
Employment status						
Working	407	5	1.2	243	12	4.9
Not working	174	10	5.7	399	52	13.0
Male: working activity						
Industry	213	3	1.4	—	—	—
Other	194	2	1.0	—	—	—
Female: work activity						
Housewife	—	—	—	369	51	13.6
Outside house	—	—	—	209	15	7.2

was also associated in both sexes with psychotropic consumption (males, $\chi^2=8.2$, d.f. = 1, $P<0.01$; females, $\chi^2=12.8$, d.f. = 1, $P<0.001$). The type of work was not relevant in the case of males, but in females we found a significantly higher use of psychotropic drugs among housewives than among those working outside the house ($\chi^2=5.2$, d.f. = 1, $P<0.05$). The social status of the respondent was not significantly related to psychotropic drug use.

Psychotropic drug use in relation to physical and mental illness

The prevalence of psychotropic drug use in relation to sex, age, and physical illness is shown in Table VI. The presence of physical illness is, in both sexes, significantly linked with psychotropic drug consumption (males, $\chi^2=8.5$, d.f. = 1, $P<0.01$; females, $\chi^2=46.9$, d.f. = 1, $P<0.001$). This pattern appears – at different levels of significance – in each age group.

The interaction between psychotropic drug use and mental illness was explored in the first-stage sample by the GHQ-60 and in the second-stage sample by the PSE-ID-CATEGO system. The relationships between drug consumption and scores on the GHQ-60 and ID are summarised in Table VII. For both males and females, psychotropic drug use tends to increase progressively with

TABLE VI

Psychotropic drug use by sex, age, and physical illness

Sex and age	*Physically ill*			*Not physically ill*		
	Number in first-stage sample	*Taking psychotropic drugs*		*Number in first-stage sample*	*Taking psychotropic drugs*	
		Number	*%*		*Number*	*%*
Males <34	27	1	3.7	152	1	0.7
Males 35–54	47	1	2.1	138	2	1.4
Males >55	127	9	7.1	90	1	1.1
Total males	201	11	5.5	380	4	1.1
Females <34	42	4	9.5	140	1	0.7
Females 35–54	116	26	22.4	109	1	0.9
Females >55	164	32	19.5	71	5	7.0
Total females	322	62	19.3	320	7	2.2

TABLE VII

Psychotropic drug use by GHQ score at the first stage of sampling, PSE-ID severity level at the second stage of sampling, and sex

	Males			*Females*		
	Total number in sample	*Taking psychotropic drugs*		*Total number in sample*	*Taking psychotropic drugs*	
		Number	*%*		*Number*	*%*
First stage: GHQ-60 score						
0–5	428	6	1.4	347	13	3.7
6–11	85	2	2.4	136	11	8.1
12–19	45	2	4.4	89	16	17.9
20+	23	5	21.7	70	29	41.4
K–S test		$D=0.51$, $P<0.01$			$D=0.33$, $P<0.01$	
Second stage: PSE-ID severity level						
1	82	0	0.0	67	5	7.5
2–4	68	4	5.9	113	16	14.2
5–8	27	5	18.5	95	33	34.7
K–S test		$D=0.43$, $P<0.01$			$D=0.29$, $P<0.01$	

TABLE VIII
Psychotropic drug use by PSE–CATEGO diagnosis and sex

PSE–CATEGO diagnosis	*Males (n = 177)*			*Females (n = 275)*		
	Number at second stage	*Taking psychotropic drugs*		*Number at second stage*	*Taking psychotropic drugs*	
		Number	*%*		*Number*	*%*
Phobic–anxiety[1]	7	—	—	52	15	28.9
Depression[2]	17	4	23.5	39	16	41.0
Other states[3]	3	1	33.3	4	2	50.0
Total psychiatrically ill	27	5	18.5	95	33	34.7
Not psychiatrically ill	150	4	2.7	180	21	11.7

1. Anxiety state; phobic state.
2. Neurotic depression; retarded depression.
3. Manic and mixed affective psychoses; schizophrenic psychoses; paranoid psychoses; borderline and doubtful psychoses; other conditions; obsessional neurosis.

the GHQ and ID scores. In both instruments, this tendency is more marked above the cut-off point and especially in the higher-severity score. The rate of psychotropic drug consumption by PSE–CATEGO diagnosis is shown in Table VIII. We found higher psychotropic drug use in the psychiatrically ill than in those not psychiatrically ill. This increase reaches significance in both males and females (males, $\chi^2=8.9$, d.f. = 1, $P<0.01$; females, $\chi^2=19.5$, d.f. = 1, $P<0.001$). It can also be seen that among subjects of psychiatric 'case' level the percentage using psychotropic drugs is very low. No analysis has been made of consumption in the different diagnostic categories due to the low figures. However, as regards depression, although there is a tendency to use more psychotropics, this is reversed by the fact that the majority of consumers use only tranquillisers (using only tranquillisers: males 83.3%, females 79.2%; Vázquez-Barquero *et al*, 1989).

Another aspect to consider is the way in which the association between physical and mental illness influences psychotropic drug consumption (Table IX). We found that the rate of consumption in respondents in whom physical and mental illness coexisted was significantly higher than that in respondents without any type of illness ($\chi^2=67.5$, d.f. = 1, $P<0.001$), and also more than that in respondents with physical illness alone (psychiatric and physical illness v. physical illness alone: $\chi^2=8.7$, d.f. = 1, $P<0.01$). In the comparison between patients with psychiatric and physical illness and those with psychiatric illness alone, the tendency was similar but did not reach significance. There was not a significant difference between those affected by physical illness alone and those with mental illness alone, but there were significant differences between each of these two groups and those without any type of illness. (Physical illness alone v. no physical and no psychiatric illness: $\chi^2=26.9$, d.f. = 1, $P<0.001$. Psychiatric illness alone v. no physical and no psychiatric illness: $\chi^2=19.7$, d.f. = 1, $P<0.001$.)

TABLE IX
Psychotropic drug use by presence or absence of psychiatric and physical illness

Illness combination	*Number in second-stage sample*	*Taking psychotropic drugs*	
		Number	*%*
Psychiatric illness and physical illness	89	32	35.9
Psychiatric illness without physical illness	33	6	18.2
Physical illness without psychiatric illness	135	23	17.0
Neither psychiatric nor physical illness	195	2	1.0

Female v. male predominance in psychotropic drug consumption

The higher prevalence of psychotropic drug use among females is maintained at a significant level for all the variables explored except for subjects of age ≤ 34, those of single marital status, those of higher educational level, and those who were physically healthy. In these groups the differences in psychotropic use disappeared because of a reduction in consumption by females.

Discussion

A detailed discussion of the extent and correlates of psychiatric morbidity detected in the Community Mental Health Survey of Cantabria, and the interaction of psychiatric morbidity with social factors and physical illness, has been presented in previous papers (Vázquez-Barquero *et al*, 1987*a*,*b*, 1988). We centre the present discussion on psychotropic consumption, focusing on three main issues: the prevalence of psychotropic use; sex differences in psychotropic use; and psychotropic use in relation to physical and mental illness.

Prevalence of psychotropic use

The results of this study indicate that 6.9% of the general population (10.7% of females and 2.6% of males) were 'currently' and on a 'regular basis' consuming psychotropic drugs. These rates are much lower than those reported in the majority of the community surveys reviewed by Williams (1979). Most of these surveys, however, applied a more diffuse methodology than the one reported here, and investigated one-year prevalence of consumption, so they are not susceptible to comparison with this survey. Studies which selected a methodological design like the one applied here and which, as in our case, investigated current psychotropic use, yielded prevalence figures just over 10% (Craig & Van Natta, 1978; Murray *et al*, 1981). In addition, the only study of a Spanish general population reported a similar rate of psychotropic consumption (total 9.3%; female 12.5%; male 7.0%; Balter *et al*, 1974). Although these rates are nearer the ones found in this survey, they are nevertheless still higher. Although under-reporting could be a possible explanation for our lower figures, the characteristics of the methodology applied for exploring drug-taking makes this source of error unlikely. An alternative explanation could rest on the rural nature of our sample. There is evidence for this in the work of other authors, in which it is seen that in rural areas there is a lower rate of prescription than in urban areas (see Gabe & Williams, 1986). As these authors indicate, three different, but complementary, explanations could account for the rural/urban differences in tranquilliser prescribing. First, the higher drug prescribing and use in urban areas may stem from urban life being possibly more stressful and less satisfactory than rural life. This situation may lead, as we have seen before (Vázquez-Barquero *et al*, 1982), to an increase of psychological and physical ill-health, and consequently to an increase of psychotropic drug use. Secondly, it may be that those in rural areas, because of cultural reasons or due to relative inaccessibility of medical services, could be more reluctant to seek medical help, and in consequence could receive fewer prescriptions. Finally, we could postulate that rural doctors, because of their work style, could be less likely to prescribe tranquillisers. The design of this study, however, does not allow us to test any of these hypotheses. Neither does it allow us to be sure that our findings could be extended to other European rural communities. We feel that this is a very relevant issue which calls for a collaborative international research project directed to verify, with a similar methodological design, urban/rural differences in mental health and psychotropic drug use.

An additional aspect to consider is that in our community a considerable proportion of psychotropic consumers are using these drugs in association with other medicines. This association, which has also been reported by others (Mellinger *et al*, 1978; Uhlenhuth *et al*, 1978), strengthens the opinion that both somatic and psychotropic drugs are often used as adjunctive treatment for disorders. This pattern of drug use may well be the result of the existing interaction between physical and mental illness detected in Spanish rural communities (Vázquez-Barquero *et al*, 1981, 1988). There is also in this community a high rate of analgesic use. This, as found in other surveys, is significantly higher in women than in men (Helman, 1986; Jefferys *et al*, 1960).

Sex differences in psychotropic use

Like other authors we found that psychotropic drug consumption is significantly higher in women than in men (e.g. Balter *et al*, 1974, Cooperstock, 1978; Williams, 1979). The predominanee of consumption by females was significantly enhanced among older subjects, and among those in the categories 'lower educational level', 'married', 'absence of work', and 'housewife', while it disappeared for younger subjects, and for those in the categories 'single marital status' and 'outside-the-house activity'. Due to the small sample figures, we have been unable to check for interactions between variables (e.g. age and marital status). Nevertheless, the findings lend some support to social-stress theories, which suggest that women's greater use of psychotropic drugs may be associated with the fact that they are more likely to be under the influence of social and family stressors, or may be because they are more sensitive to stress (Cooperstock, 1978; Kessler, 1979; Cafferata *et al*, 1986). There is now evidence to suggest that while marriage has a protective effect against mental illness in men, it acts as an important source of stress in women (Weissman & Klerman, 1977; Bebbington *et al*, 1981). The work of Brown & Harris (1978) and of Bebbington *et al* (1981) demonstrated that in married women the presence of children under 14 years of age tends to be linked with unemployment, and that both these factors are directly related to the development of emotional disorders. Brown & Harris (1978) interpreted this association by postulating that the presence of these factors limit a woman's ability to develop adequate role identity, intimate interpersonal relationships and good self-esteem. All this, they say, will increase in women the chance of a general hopelessness, from which mental illness will arise.

It could be postulated that mental illness is the mediating mechanism between stress and psychotropic consumption. Our data, however, do not confirm this entirely since they show that the female predominance of consumption is higher in the group without mental illness. Our findings, therefore, appear to support the opinion put forward by authors who say that sex differences in psychotropic drug use cannot be accounted for solely by women being more mentally ill (Cooperstock, 1971; Murray *et al*, 1981).

Psychotropic use in relation to physical and mental illness

A number of studies have found a relationship between psychotropic consumption and emotional disorders as measured by different psychopathological instruments (Harris *et al*, 1977; Mellinger *et al*, 1978; Uhlenhuth *et al*, 1978; Murray *et al*, 1981). This has been confirmed in our study by the GHQ-60 data in the first stage of the survey and by the PSE-ID data in the second stage. We could identify a general tendency for psychotropic use to increase with the scores on both instruments, even below threshold. This tendency, however, becomes more marked above the cut-off point for 'caseness', and especially in the highest-severity scores. This suggests that 'caseness' may not be the only factor relevant to consumption, and that we have also to take into account the presence and severity of symptomatology. Our data show, in addition, that a certain proportion of respondents without psychopathological symptoms (ID score 1, GHQ score 0-5) are taking psychotropic drugs. These findings, which concur with those of Murray *et al* (1981), are in our case due to the presence of physical illness in these respondents (Vázquez-Barquero *et al*, 1988). An additional point is that in our community only a small proportion of subjects of 'case' status are consuming psychotropic drugs (males 18.5%, females 34.7%). This low rate of psychotropic use by the mentally ill of our community, which is almost equal to that found by Murray *et al* (1981) and Mellinger *et al* (1978), has important health implications, more so if we consider that our findings, although based on small sample figures, appear to suggest that depressives are exclusively taking anxiolytics (Vázquez-Barquero *et al*, 1989). Thus our data appear to confirm that in the community only a small proportion of the emotionally disturbed are using psychotropic drugs, and that anxiolytics are very often prescribed as the treatment for depression (Mellinger *et al* 1978; Gullick & King, 1979; Murray *et al*, 1981).

Although psychopathology should be the main reason for psychotropic consumption, the fact is that in our survey these drugs are also widely used in physical conditions, thus confirming the findings of other authors (Mellinger *et al*, 1978; Williams, 1978). It has also been shown that the coexistence of physical and psychiatric illness accounted for substantially more psychotropic use than did psychiatric or physical illness alone (Mellinger *et al* 1978; Uhlenhuth *et al*, 1978; Williams, 1978). Our results tend to confirm this, since they show that the joint presence of physical and mental illness generates a significant increase in consumption, while the absence of both types of illness is indicative of almost no use of psychotropic drugs. For physical and for mental illness alone, the rates of consumption are intermediate and almost equal.

Conclusion

We have presented data illustrating that - in addition to mental illness - the presence of physical disease and of certain sociological factors significantly conditions the use of psychotropic drugs in the community. The finding that a vast majority of those emotionally disturbed may not be taking psychotropics, or may be consuming them in an inadequate manner, has important health implications and should also be emphasised. The consequence of these findings are twofold: first, more attention needs to be directed to the analysis of the complex mechanisms which condition psychotropic drug prescription and use in different medical and community settings; and second, the time is ripe for the development of health intervention strategies geared to improve the prescription and consumption of psychotropic drugs. This should involve the development of much larger and intensive multinational 'research-intervention' studies, geared (a) to identifying the factors which condition the prescription and consumption of psychotropic drugs in areas which differ in the extent to which they can be described as rural or urban in a sociological sense, and (b) to developing health and educational strategies directed at improving these prescribing and consuming habits. Subsequent monitoring and surveillance of the results of the 'intervention' strategies should be integrated into such 'research-intervention' studies.

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Anorexia Nervosa in a Swedish Urban Region

A Population-Based Study

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The total population of 15-year-olds in Göteborg, Sweden, were screened in 1985 for anorexia nervosa using brief questionnaires, growth charts and individual school nurse reports. An accumulated frequency of anorexia of 0.84% for girls up to and including 15 years of age was obtained, with 85% of the cases fulfilling DSM-III-R criteria. Boys were affected just over one-tenth as often as girls. The frequency of anorexia nervosa appeared to be much higher in private than in comprehensive schools. The peak age of onset seemed to be 14 years.

The incidence of anorexia nervosa (AN) has been estimated in a number of studies throughout the last 30 years. Kendell *et al* (1973) reported on the incidence of AN in three case registers: those for North East Scotland, 1966–69; Monroe County, New York State, 1960–69; and Camberwell, London, 1965–71. The estimates of the annual overall incidence varied from 0.37 per 100 000 in Monroe County, to 1.6 per 100 000 in North East Scotland. The Camberwell register gave an average annual incidence of 0.66 per 100 000 population. The age-specific rates for females aged 15–34 years were 0.8 per 100 000 (Monroe County), 10.8 per 100 000 (North East Scotland), and 4.1 per 100 000 (Camberwell). In all three areas the number of cases reported in the second half of the time span in question was greater than that in the first.

Jones *et al* (1980) calculated the mean annual incidence rate for Monroe County for the period 1970–76 to be 0.64 per 100 000. Age-specific rates for females were 1.54 per 100 000 for age under 15 years, 3.26 per 100 000 for age 15–24 years, and 0.96 per 100 000 for age 24–34 years.

From the register in North East Scotland, Szmukler *et al* (1986) reported an average annual incidence of 4.06 per 100 000 for the period 1978–82. The rate for females aged 16–25 years was 0.30 per 1000. The peak annual incidence rate, 0.5 per 1000, was for females aged 18 years.

From the canton of Zurich in Switzerland, Willi & Grossmann (1983) reported an annual incidence among female in-patients of 0.38 per 100 000 in 1956–58, increasing to 1.12 per 100 000 in 1973–75.

In a study of a region of southern Sweden during 1931–60, Theander (1970) reported an overall annual incidence in females of 0.24 per 100 000, with a rise to 0.45 per 100 000 for the last decade.

From the Netherlands, Hoek & Brook (1985), using a local psychiatric case register, reported for the period 1974–82 an annual incidence rate of 5.0 per 100 000, and a rate of 37.1 per 100 000 for females aged 15–24.

A retrospective case-record review of referrals to psychiatrists in Glasgow (Leighton & Millar, 1985) for 1979–83 identified 122 patients with eating disorders, 97 of them having AN (three of them 'partial syndrome'). Of the 122 patients, five were males. Glasgow has a catchment population of about one million.

Using the Eating Attitudes Test (Garner & Garfinkel, 1979) for initial screening, followed by interviews with high scorers, Mann *et al* (1983) found no cases of AN in a state-school population in London of 262 girls aged 15 years, and Szmukler (1983) in six private schools found prevalence figures of one in 120 girls aged 14–18 years, and one in 90 girls aged 16–18 years.

In 1972–74, Crisp *et al* (1976) surveyed a selected group of schools in London in respect of the occurrence of AN. The group comprised seven private girls' schools, one comprehensive girls' school, and the female pupils in one mixed-sex comprehensive school. In the private schools, the prevalence was one severe case per 100 girls aged 16 and over, and one per 500 girls 15 years and under. In the two comprehensive schools there was only one case identified, and that one was in the age group 16 years and over.

In Sweden, Nylander (1971) performed a questionnaire study in a school population (1129 boys and 1241 girls) and found that dieting was commonplace among teenagers. Among the dieters there were nine female cases of AN aged 16–25 years. A prospective follow-up of a selected group of the dieters gave six more cases (Schleimer, 1983).

The total of 15 represented 1.2% of the 1241 girls.

Anorexia nervosa is believed to be a syndrome of Western cultures, although cases have been reported from Japan (Miyai *et al*, 1975) and Singapore (Ong *et al*, 1982). From Malaysia (Buhrich, 1981), a selective study, based on reports from private psychiatrists, suggested that the condition was rare in that country. From the developing countries there is one case report (Nwaefuna, 1981) of a Nigerian girl. The incidence in the black population of Western countries is believed to be extremely low (Pumariega *et al*, 1984).

Incidence among males is estimated at 5–10% of the total incidence. The proportion of males in some of the studies mentioned above ranges from 1:6 to 1:15 (Kendell *et al*, 1973; Jones *et al*, 1980; Szmukler *et al*, 1986). Of more than 300 patients reported in the literature during 1970–80, only 6.4% were males (Vandereycken & Van den Broucke, 1984).

Our study reports on the prevalence of anorexia nervosa in a Swedish urban area in 1985.

Method

Definitions used

Anorexia nervosa: full syndrome (AN full) was diagnosed (a) in all subjects fulfilling the criteria of DSM–III (American Psychiatric Association, 1980) for AN, which require a real or projected weight loss of 25% or more (AN DSM–III), and (b) in those subjects fulfilling all but the weight criterion of DSM–III and having a real or projected weight loss of more than 15% (AN DSM–III–R) (American Psychiatric Association, 1987).

Anorexia nervosa: partial syndrome (AN partial) was diagnosed when subjects fulfilled DSM–III criteria apart from (a) having real or projected weight loss of 15% or less, or (b) having anorectic behaviour which, in spite of major weight loss, was not considered to be extreme.

Bulimia nervosa (BN) was diagnosed in all subjects fulfilling DSM–III criteria for bulimia nervosa.

Other major psychiatric disorders (not primarily eating disorders) were diagnosed in accordance with DSM–III criteria.

Informing others about the study

All school nurses and doctors in the area (the city of Göteborg on the west coast of Sweden, population c. 450 000) were informed of the study and its goals at a special seminar. All paediatricians were informed at a special lecture, and all child and adolescent psychiatrists at a separate seminar. All parents and children were informed by letter. The first author also talked on an individual basis with each of the 36 school nurses.

Population screening

The aim of the study was to reach all children born in 1970 and living in Göteborg on 31 December 1985 who had or had had AN before their 16th birthday.

All children attending the eighth grade of all Göteborg schools on 31 May 1985 were screened. Ninety-nine per cent of these youngsters were born in 1970: their age range at that time was thus 14.5–15.5 years. In all, there were 4291 children who attended the eighth grade. These children comprised our study population. Also, every effort was made to trace any relevant information concerning children born in 1970 who were not attending the eighth grade.

There were 11 children whose parents declined to have their child's growth chart examined by the authors. The charts of these 11 children were considered normal by the school nurse. This means that 100% of the population were included in the screening.

Mentally retarded children attending special schools were not included in this study. However, all mentally retarded children born in 1970 were simultaneously screened for psychiatric disorder by the second author (Gillberg *et al*, 1986). No case of AN was found in this sub-population.

Procedure

All growth charts for each individual ($n = 4291$; 2136 girls and 2155 boys) were collected from the school health services and scrutinised by one doctor (MR). All 4291 children had been weighed and measured in the spring term of 1985.

All 4291 youngsters completed an eight-item questionnaire covering such topics as food interests, weight, desire to lose weight, and menstrual problems. All growth charts and questionnaires were coded and the doctor who examined them had no other information about the particular child analysed.

Assignment for further study

The following children were assigned for further study: (a) all those fulfilling the DSM–III (1980) weight criterion (i.e. a real or projected weight loss of more than 25%); (b) all those showing severe rapid weight loss but not meeting the DSM–III weight criterion; (c) all those bordering on (a) or (b) who admitted on the questionnaire to having symptoms raising suspicion of anorexia; (d) all those who were rapidly losing weight in relation to height (i.e. who had a rapidly decreasing Quetelet index (weight (kg)/(height (m))^2 (Llewellyn-Jones & Abraham, 1984); (e) all those with secondary amenorrhea; and (f) all those who had always been very thin and who admitted to wanting further weight loss on the questionnaire. Altogether 330 girls (15.5% of all girls) and 55 boys (2.6% of all boys) were selected in this way.

These 385 children, who had all raised some suspicion of suffering from symptoms of AN or suspected AN, were repeatedly checked for weight by the school nurses (who were continuously contacted by the principal school nurse) throughout the next year; that is, during the whole of the period up to 31 May 1986. Others who had not been identified previously, but who were discovered in the autumn of 1986, were also enrolled in the study.

For all 385 children, one of the authors (MR) then interviewed by telephone (once or several times) the school nurse, who had talked with and personally examined the child. The school nurses were also asked to report any pupil not included in this group who raised suspicion of suffering from AN. In this way six more children were found. The authors then again met all the nurses on one or more (usually two) occasions to discuss the study and to inquire about possible suspected cases.

After these interviews and a final thorough analysis of the growth charts, there remained 44 children (39 girls and 5 boys) who had shown or were showing problems which might well be compatible with a diagnosis of AN. All these children and their parents were contacted by MR for participation in the diagnostic study. Three further children attending the eighth grade were found, but they belonged to an older age group and will be reported elsewhere.

One girl refused participation in the diagnostic study, leaving 43 children for neuropsychiatric examination.

Register search and screening among paediatricians and child psychiatrists

In Sweden, children aged 15 years or under apply for medical/psychiatric help at paediatric or child psychiatric clinics. The registers of the Göteborg paediatric and child psychiatric clinics were searched, and all paediatricians and child psychiatrists liable ever to get in touch with AN patients were asked if they knew of any child living in Göteborg and born in 1970 who had currently or had ever had symptoms raising suspicion of AN. No new cases hitherto undetected in the population screening were found in this way.

Boarding schools

Swedish boarding schools for children of normal intelligence are extremely few. Less than 0.05% of the whole Swedish population born in 1970 attended such schools during the course of this study. One of these was a girl who was reported to have AN, but it is unlikely that she resided in Göteborg, although we cannot be completely certain in this respect.

Diagnostic study

All children, except one examined by a child psychiatrist (CG), raising suspicion of suffering from AN were seen by one psychiatrist (MR), who carried out a 2–4 hour assessment, including interview and examination of each child individually, and interview with the mother. All relevant medical-record data were reviewed. A medical history comprising some 1000 items (including social, psychological and medical data) was taken.

Results

Diagnoses

Of the 43 children (38 girls, 5 boys) examined neuropsychiatrically, ten (one boy and nine girls) were judged to be psychiatrically healthy in all respects. The remaining 33 were assigned to (no more than) one of the following diagnostic groups (Table I): AN full; AN partial; BN; other major psychiatric disorder.

AN full. Ten girls and two boys fulfilled the DSM–III criteria for AN (AN DSM–III). Another four girls were also diagnosed as suffering from AN (AN DSM–III–R).

AN partial. AN partial syndrome was diagnosed in three girls.

BN. Three girls fulfilled the DSM–III criteria for bulimia nervosa.

Other major psychiatric disorder. In nine girls and two boys the following disorders were diagnosed: major depression ($n = 3$), emotional disorder ($n = 3$), conduct disorder ($n = 2$) and personality disorder ($n = 3$).

The girl who refused participation had AN DSM–III–R according to medical records and results obtained by interview with the school nurse.

TABLE I
Children assigned to diagnostic study

	Number	*Boy: girl ratio*	*% of population*
Number of children assigned for study	44	5:39	1.03
Children already in psychiatric treatment or referred for such treatment because of DSM–III diagnosis of AN (also examined by author)	3	0:3	0.07
Other children fulfilling DSM–III criteria for AN examined by author	9	2:7	0.21
Children fulfilling DSM–III–R criteria for AN examined by author	4	0:4	0.09
Children fulfilling DSM–III–R criteria for AN already in psychiatric treatment or referred for such treatment (not examined by author)	1	0:1	0.02
Children with partial AN examined by author	3	0:3	0.07
Children with BN according to DSM–III criteria examined by author	3	0:3	0.07
Children with other major psychiatric diagnoses (DSM–III)	11	2:9	0.26
Children without major psychiatric problems	10	1:9	0.23

Prevalence of AN

Altogether 17 children had AN full syndrome, and another three had AN partial syndrome. This corresponds to population frequencies for AN full syndrome of 0.70% for girls 15 years or under and 0.09% for boys, and for AN full and partial syndromes combined 0.84% for girls and 0.09% for boys (Table II). Accumulated prevalence (i.e. the frequency of children who at the time of examination had or had had the disorder) of AN for children, boys and girls combined, aged 15 years or under, was 0.47%. Of the total group with AN, full or partial syndromes, 60% fulfilled DSM-III criteria for AN.

The population-corrected girl:boy ratio was 9.1:1.

Age of onset

Six girls had an onset of AN at age 13 years, eight girls and two boys at age 14 years, and four girls had their first symptoms of AN at age 15 years.

In two of the girls and the two boys, the onset of AN occurred in early puberty. The other girls thus presented with secondary amenorrhea.

Other epidemiological data

At the start of the study, four children were already known to the Child and Adolescent Psychiatric Clinic, and by the end, five more had been treated in child psychiatric services.

Two of the 18 girls with AN (both with AN full syndrome) had a severe metabolic disorder, which had preceded the onset of AN by a month in one case (with diabetes mellitus) and three years in the other (with hypothyroidism treated with hormones and now euthyroid). No other AN case had any severe medical problems.

All the girls and boys with AN were of normal or above normal intelligence.

Only 4.5% of the whole population studied attended private schools. Of all the AN patients in Göteborg, 15% were recruited from such schools (all of these had AN full syndrome). Of 20 AN patients, 7 (35%) came from schools in poorer areas, and 13 from more privileged parts of the city. In the whole screened population, 35.3% (1513/4291) came from schools in poorer areas.

TABLE II

'Accumulated prevalence' of AN among 15-year-olds in Göteborg, Sweden, 1985 (% of population)

Diagnostic category	*Boy prevalence*	*Girl prevalence*	*Total prevalence*
AN DSM-III	0.09	0.47	0.28
AN DSM-III-R	0.00	0.23	0.12
AN partial syndrome	0.00	0.14	0.07
AN total (partial or full syndrome)	0.09	0.84	0.47

Discussion

In previous studies of the prevalence of AN, the rate of occurrence of the disorder has been observed to increase over time. In this prospective study of AN we have investigated a non-selected population of children 15 years and under in a defined area. To our knowledge there exists only one relatively comparable epidemiological study concerning the prevalence of AN in this age group, namely the study of Crisp *et al* (1976). These authors found a prevalence of 0.2 per 100 in schoolgirls 15 years and under, compared with the prevalence in this study of 0.70 per 100 with AN DSM-III or DSM-III-R.

The two populations are not quite comparable, however, in that the London population was drawn from a selected group of private schools where one would expect a high prevalence of AN. In this study, 15% of the AN patients came from private schools. On the other hand, the AN cases in the study of Crisp *et al* were all very severe, with all the girls having lost >30% of their body weight.

In our study, children born in 1970 were studied at age 15 years. The assumption is that at this early age the school nurses have close contact with the pupils, which would tend to eliminate non-participation. Also, in that age group, school attendance is almost universal. We found the peak age of onset to be 14 years. Current follow-up of this age group by telephone interviews with school nurses and child psychiatrists does not suggest a higher incidence among 16-year-olds than among 15-year-olds. Some earlier studies (Crisp & Stonehill, 1971; Szmukler *et al*, 1986) have reported a peak age of onset of 18 years. Most studies so far have been based on hospital populations. Ours was a study of prevalence in the general population. The Szmukler study of referral cases indicated a peak female incidence of 0.5 per 1000 among 18-year-olds. Our data suggest that the peak female incidence might occur among 14-year-olds and that it is much higher (c. 3.7 per 1000). We have observed that many of these children are never referred to child and adolescent psychiatric clinics or to paediatric departments. (In our study this applied in 11 of the 20 cases with AN.) It may be that severe cases often come to the attention of clinics only after several years of illness, which in turn may lead to the impression that age of onset is higher than it actually is.

We agree with Szmukler (1985) that subjects with a partial syndrome should be included in epidemiological studies of AN. If one regards partial AN as AN of a less severe degree, one would expect such cases to outnumber the more clear-cut ones. In fact they do in some studies using a questionnaire followed up by interview (Szmukler, 1983; Mann *et al*, 1983).

With our method, only partly relying on subjects' admitting to anorectic symptoms in the brief questionnaires, and mostly built on clinical data such as growth charts and school nurses' and doctors' observations, we expected to find severe and moderate cases, and not many on the borderline. Even the children reported here as having partial syndromes had severe and conspicuous symptoms.

The sex ratio accords well with that of other studies, but does not allow for conclusions, the boys being too few.

The rate of occurrence of bulimia nervosa is low in this study. We were not aiming to investigate that syndrome, which means that our figure for bulimia nervosa is certainly not a population-based one.

The attrition in this study is extremely low, and so the results should be of particular interest from the epidemiological point of view.

In summary, this population-based study of all 15-year-olds in a Swedish urban area yielded a total prevalence of AN in girls up to and including age 15 years of 0.84%. Eighty-five per cent of the cases fulfilled DSM-III-R criteria for the disorder. The prevalence among boys was only just over one-tenth of that among girls. The results indicate that AN is even more common in the general population than has been thought by previous writers in the field. Detailed clinical data about the patients enrolled in this study will be presented in a forthcoming paper.

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Prevalence of Childhood and Adolescent Depression in the Community

Ontario Child Health Study

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Data from a cross-sectional community survey of 2852 children were used to provide estimates of the prevalence of a 'DSM-III-like' major depressive syndrome in children aged 6 to 16. The severity of symptoms required to define a 'case' was varied to generate three levels of diagnostic certainty (DC). The overall estimates of prevalence made with high DC were 0.6% for pre-adolescents and 1.8% for adolescents. Corresponding rates determined with medium DC were 2.7% and 7.8%, whereas the figures for low DC were 17.5% and 43.9%. Utilisation of mental health and social services, comorbidity (combined disorders), poor school performance, problems in getting along with others and need for professional help all increased as diagnostic certainty increased. There was wide disagreement in data supplied by the different groups of respondents, i.e. parents, teachers and adolescents.

There is growing interest in the prevalence of childhood depression in the general population. In the last ten years prevalence rates for depression have been given for the pre-adolescent age group in at least five studies (see below) and for the adolescent age group (Table I) in at least 14 studies. There have also been two recent reviews of the literature (Angold, 1988; Fleming & Offord, 1989).

Two major issues in the measurement of childhood depression are brought to light in the published studies. The first is the issue of diagnostic certainty, or 'caseness'. While comparable diagnostic criteria for major depression were used in five studies of the pre-adolescent age group, actual 'caseness' was defined in different ways. These included the application of diagnostic criteria alone to elicited symptoms (Kashani & Simonds, 1979; McCracken *et al*, 1989), the application of diagnostic criteria plus consideration of impairment in social functioning (Kashani *et al*, 1983), severity and duration of symptoms (Anderson *et al*, 1987), and responses to a depression scale (Velez *et al*, 1989). This lack of consistency in case definition makes comparison of estimates of prevalence in different studies very difficult, as evidenced by the wide range of estimates obtained in the above studies (from 0.5% (Anderson *et al*, 1987) to 2.7% (McCracken *et al*, 1989)).

The second important issue raised is that of respondent disagreement. Parent–child disagreement in identifying depressive disorders has been demonstrated with highly structured interviews (Edelbrock *et al*, 1986; Kashani *et al*, 1985; McCracken *et al*, 1989; Reich *et al*, 1982; Sylvester *et al*, 1987), with a semistructured interview (Weissman *et al*, 1987; Angold *et al*, 1987) and with check-lists (e.g. Weissman *et al*, 1980; Kazdin *et al*, 1983; Kazdin, 1987). Teacher–child and teacher–parent disagreement have been examined only for check-lists. Non-significant or significant but low correlations have been found between teacher-rated and child-rated depression scales (Sacco & Graves, 1985; Saylor *et al*, 1984; Reynolds *et al*, 1985; Wierzbicki, 1987), while moderately significant correlations have been found between teacher-rated and parent-rated scales (Reynolds *et al*, 1985; Wierzbicki, 1987).

In four of the five prevalence studies mentioned earlier, agreement between groups or among groups of respondents was not dealt with, since information from sources was combined in some way to arrive at the depressive diagnoses. In the fifth study (McCracken *et al*, 1989) the child-identified rate of major depression (2.7%) was twice as high as the parent-identified rate (1.3%). Teacher-identified estimates of prevalence were not reported for any study.

Table I presents studies of the prevalence of depression in adolescents. The most common approach to measuring depression in this age group has been to use self-report check-lists, the Beck Depression Inventory (BDI) and the Center for Epidemiologic Studies Depression Scale (CES–D), with the adolescent as the sole data source. Two studies did use adolescents and their parents as data sources but neither study presented estimates of prevalence separately by source, nor did either study comment on the agreement between informants (Kashani *et al*, 1987; Velez *et al*, 1989).

A score of 16 or more on both the BDI (Beck, 1967) and the CES–D (Myers & Weissman, 1980) has been found to correspond to the presence of a major depression in adults. When this cut-off score is applied to adolescents (Table II), the resulting prevalence rates are implausibly high. The overall

TABLE I

Community studies of the prevalence of depression in adolescents

Instruments	n	*Age(s)*	*Prevalence (%) of depression*		
			Overall (>16)	*Moderate (16–23)*	*Severe (>24)*
I. Self-report check-lists					
(a) *Beck Depression Inventory (BDI)*					
Albert & Beck (1975)	63	11–15	36.5[1]	33.3	3.2
Teri (1982)	568	14–17	32.0	27.0	5.0
Reynolds & Coats (1982, unpublished data)[2])					
Study 1	675	14–18	17.0	12.0	5.0
Study 2	735	14–18	11.0	6.0	5.0
Kaplan *et al* (1984)	385	11–18	8.6	7.3	1.3
Siegel & Griffin (1984)	99	12–18	20.2	—	—
Gibbs (1985)	116	14–18	23.0	—	—
Sullivan & Engin (1986)	103	grades 10 & 11	32.0[1]	26.0	6.0
Kaplan *et al* (1987)	577	12–18	21.9	14.6	7.3
Weinberg & Emslie (1988)	3294	mean 15.7	18.1	—	—
(b) *Centre for Epidemiologic Studies – Depression Scale (CES–D)*			*% with score >16*	*% with other depression*	
Schoenbach *et al* (1982)	384	12–15	almost 50	2.9	('RDC-like' syndrome)
Chien & Cheng (1985)	2888	High-school students	40		—
Wells *et al* (1987)	424	16–19	33	16 (duration ≥3 days) 2 (duration ≥5 days)	
II. *Highly structured diagnostic interviews*				*Prevalence (%) of major depressive disorder*	
Deykin *et al* (1987)	(same sample as above, Wells *et al*, 1987)			6.8 (lifetime)	
Kashani *et al* (1987)	150	14–16		4.7 (current)	
Velez *et al* (1989)	456	13–18		3.7 (current)	

1. The short (13-item) BDI was used; scoring was 8–39 for overall depression, 8–15 for moderate and 16–39 for severe depression.
2. One item omitted from BDI.

rates of moderate to severe depression in studies using the BDI range from 8.6% (Kaplan *et al*, 1984) to 36.5% (Albert & Beck, 1975). Rates of depression in studies using the CES–D range from 33% (Wells *et al*, 1987) to "nearly half of the sample" (Schoenbach *et al*, 1982). With the BDI studies, rates are lower and more plausible when only 'severe' cases of depression are included. In two of the CES–D studies, the authors attempted to define a depressive syndrome more in keeping with current diagnostic systems. For example, in one study (Schoenbach *et al*, 1982), only items that corresponded to a major depression as defined by Research Diagnostic Criteria were counted. As a result, the depression rate dropped from almost 50% to 2.9%. In the other study (Wells *et al*, 1987), the depression rate dropped from 33% to 16% when only symptoms lasting three or more days of the week were counted. The rate fell further to 2% when a duration of 5 to 7 days was required for all symptoms.

Some preliminary work has been done with structured interviews with adolescents (Deykin *et al*, 1987; Kashani *et al*, 1987; Velez *et al*, 1989). The first study suffered a large sample loss and the sample was not representative of the general population. In the second study, sample size was determined by budgetary limitations and was too small to generate precise estimates of prevalence. While the third study was large and suffered minimal sample loss, the issue of parent–child agreement was not dealt with.

The purpose of the present study is to expand on the current state of knowledge about childhood depression in three ways. First, we present estimates of prevalence of major depressive symptoms for a large, general population sample that includes both pre-adolescents and adolescents. Second, we are the first to deal with the issue of respondent disagreement by reporting separate estimates of prevalence for parent-identified and teacher-identified depression in pre-adolescents and for parent-identified and self-identified depression in adolescents.

Finally, we explore the issue of 'caseness' by examining five external validators of the depressive syndrome at each of three levels of diagnostic certainty.

Method

The Ontario Child Health Study (OCHS) was an interview survey of 1869 families, including 3294 children aged 4 to 16. It was carried out to determine the prevalence of psychiatric disorders and chronic medical problems in Ontario children, and to obtain information on the utilisation by them of mental health, social, correctional and specialised educational services. For the purposes of the present study, data on children aged 4 and 5 were excluded ($n = 442$). This was done for two reasons. First, we wanted to be able to compare our results with the studies already discussed which have not included children younger than six, and second, teacher data were not available for most children aged 4 and 5. The survey methodology and measurements have been described elsewhere in detail (Boyle *et al*, 1987) and are summarised here.

Sampling design

The target population of the OCHS included all children born from 1 January 1966 to 1 January 1979 whose usual place of residence was a household dwelling in Ontario. The survey excluded three groups of children representing 3.3% of the population of children aged 4 to 16 years: those children living on Indian Reserves; those in collective dwellings such as institutions; and those resident in dwellings constructed after 1 June 1981 (census day). The sampling unit consisted of all household dwellings listed in the 1981 census of Canada; the sampling frame was the 1981 census; and the sampling selection was done by stratified, clustered, random sampling from the census file of household dwellings (Statistics Canada, 1982).

The major strata for the survey consisted of the four administrative regions of the Ontario Ministry of Community and Social Services (MCSS), with each region subdivided into three strata on the basis of the 1981 population: large urban areas with more than 25 000 population; small urban areas with population 3000 to 25 000; and rural areas of less than 3000 population. A simple random sample of households was selected from all urban areas within each MCSS region while a two-stage sampling procedure was used in small urban and rural areas. In the first stage, areas or clusters were selected; in the second stage, households were selected – both with a known probability. Statistics Canada interviewers (employed by the federal government to collect data for the Census of Canada and the Canada Labour Force Survey and other government reports) visited all sampled households to screen for eligibility, and conducted home interviews with the female head of eligible households. The survey was carried out during January and February 1983. Of all eligible households, 91% agreed to participate; only 3.9% refused to be interviewed.

Survey measures

The survey investigated four childhood disorders – conduct disorder, hyperactivity, emotional disorder (neurosis) and somatisation. Conduct disorder and hyperactivity were based on the DSM–III criteria for conduct disorder and attention deficit disorder with hyperactivity (American Psychiatric Association, 1980). Emotional disorder or neurosis combined elements of DSM–III categories of over-anxious disorder, major depressive disorder and obsessive–compulsive disorder. Somatisation was defined with reference to DSM–III and included two criteria – distressing recurrent somatic symptoms without evident physical cause and perception of oneself as sickly. The Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983) furnished the basic pool of items for measuring the diagnostic criteria with some additional items generated to describe adequately each criterion. The resulting check-list was termed the Survey Diagnostic Instrument (SDI). The SDI asks about symptoms occurring at present or in the preceding six months. Each item has three response categories: never or not true, sometimes or somewhat true, and often or very true, for which scores of 0, 1 and 2 were assigned. The items used to measure a disorder were grouped together and their responses summed to form a scale. In a separate study (Boyle *et al*, 1987), cut-off scores for diagnosis were established. Similar check-lists were completed by parents, teachers and adolescents. Responses by parents and teachers were used to assess disorder in children aged 4 to 11 and responses by parents and adolescents were used to assess disorder in adolescents aged 12 to 16. The teachers completed forms for the older age group at too low a rate for use in measuring disorder.

Measure of depression

All the criteria required by DSM–III for a diagnosis of major depressive disorder are dealt with by SDI items. This is not true for dysthymic disorder, which we did not attempt to measure. Unfortunately, the SDI assesses whether symptoms are present now or have been present in the last six months, and does not enquire specifically about the last two weeks, as required by DSM–III. For this reason we could only measure a 'DSM–III-like' major depressive syndrome. In accordance with DSM–III, we diagnosed major depressive syndrome where the child or adolescent had a depressed mood plus four or more additional depressive symptoms:

Overeating (parent and youth forms only) *or* poor appetite, not hungry
Trouble sleeping *or* sleeps more than most children during day and/or night (parent and youth forms only) *or* sleeps in class (teacher form only)
Has trouble enjoying self

Feels worthless or inferior *and/or* feels too guilty
Can't concentrate or pay attention for long
Deliberately harms self or attempts suicide *and/or* talks about killing self
Underactive, slow moving, or lacks energy (parent and teacher forms only) *or* can't sit still, restless or hyperactive (parent and teacher forms only)
I don't have much energy (youth form only) *or* I have trouble sitting still (youth form only)

Diagnostic certainty was manipulated by varying the severity of symptoms required: sometimes or somewhat true (score 1) v. often or very true (score 2). This resulted in three different levels of diagnostic certainty (DC): high (core symptom score 2, other symptom scores 2); medium (core symptom score 2, other symptom scores 1 or 2); and low (core symptom score 1 or 2, other symptom scores 1 or 2).

Validating measures

Validation of 'caseness' in psychiatry is hampered by the lack of acceptable gold standards (Vaillant & Schnurr, 1988). We chose measures of service utilisation, impairment and need for treatment because they were available and because we felt they would be meaningful external validators of a depressive syndrome. The following five measures were used:

(a) *Utilisation of mental health/social services (MH/SS).* This was based on parental report that the child, 6 to 16, was the focal point of a consultation in the last six months with staff from a mental health service (i.e. a mental health clinic, or private practitioner such as psychiatrist, psychologist, social worker), from a social service (i.e. the Children's Aid Society or the Family Service Association), from a service linked to the judiciary (i.e. the courts or the judiciary or after-care officer) or some other mental health/social/correctional service not included above.

(b) *Comorbidity.* This was based on the coexistence with depression of one or more of the original OCHS disorders (conduct disorder, hyperactivity, emotional disorder, somatisation).

(c) *Poor school performance.* This was based on parental report of the child's school performance in the last six months on the basis of a five-point rating from 'not well at all' to 'very well'.

(d) *Need for professional help.* This was based on parent or teacher report for children aged 6 to 11 and parent or youth report for children aged 12 to 16, that the child or youth had emotional or behaviour problems over the last six months for which it was felt professional help is or was needed.

(e) *Problems in getting along with others.* This was based on parent report for children aged 6 to 11 and youth report for children aged 12 to 16, that the child or youth had frequent problems in the last six months in getting along with his/her teacher(s), other children or his/her family.

Statistical analysis

Responses for estimates of prevalence were weighted to reflect the household probability of selection, its size and the age and male/female distribution of children (Boyle *et al*, 1987). Tests of statistical significance were based on actual (unweighted) responses. Weighting individual responses had little impact on estimates of prevalence (Offord *et al*, 1987). Design effects were calculated for the loss of precision attributable to clustering within families, and were found to be small. A loglinear model (Schlesselman, 1982) was used to model the relationship between age (6 to 11, 12 to 16), sex of the child and the prevalence of depression for each level of diagnostic certainty. To assess the bivariate relationship between depression and the external validators χ^2 tests were used. Missing and incomplete check-lists reduced the sample size for analysis from 2852 to 2368 for high DC, to 2386 for medium DC and to 2126 for low DC. Non-return of forms by teachers accounted for most of the loss. Bias was not evident, in that children with teachers as sources of data did not differ significantly on a wide range of sociodemographic variables from children without teachers as sources of data.

Results

Table II presents the overall prevalence rates of a 'DSM-III-like' major depressive syndrome, with data sources combined for each level of DC. For all four categories grouped according to age and sex of child, the prevalence rates for depression increased as DC decreased. For example, for children aged 6 to 11, the overall prevalence was 0.6% for high DC, increasing to 2.7% for medium DC and to 17.5% for low DC. For children aged 12 to 16 the corresponding rates were 1.8%, 7.8% and 43.9%.

There was a significant effect of age for all three levels of DC, with higher rates in adolescents (high DC, $\chi^2=5.77$, $P<0.05$; medium DC, $\chi^2=27.63$, $P<0.001$; low DC, $\chi^2=9.69$, $P<0.01$). Sex of child was only significant for the low DC group, where a three-way interaction of depression, age and sex of child was found. This interaction is accounted for by the finding that females had a higher prevalence rate for depression than males in the adolescent age group (52.4% v. 35.9%), but not in the pre-adolescent age group (17.5% for both sexes).

Table III presents separate prevalence rates for each informant, and for depression identified by both informants. In the high DC group, parents and teachers identified similar numbers of children as depressed, whereas teachers identified more children as depressed than did parents in the medium DC group, and parents identified more children than did teachers in the low DC group. For all levels of DC, adolescents identified themselves more often as depressed than did their parents. Except for the low DC group, children and adolescents were almost never identified as depressed by both informants.

Results pertaining to the validating measures are presented in Table IV. For all five measures, depressed subjects were significantly more likely than non-depressed

TABLE II

Weighted prevalence (per 100) of depression, cross-classified according to age, sex of child and level of diagnostic certainty

Level of diagnostic certainty	*Age*	*Sex*	n *(unweighted)*	*Prevalence per 100*
High	6–11[1]	Male	568	0.7
		Female	585	0.5
		Total	1153	0.6
	12–16[2]	Male	608	1.2
		Female	607	2.3
		Total	1215	1.8
Medium	6–11[1]	Male	569	2.5
		Female	587	2.9
		Total	1156	2.7
	12–16[2]	Male	609	6.8
		Female	621	8.8
		Total	1230	7.8
Low	6–11[1]	Male	492	17.5
		Female	507	17.5
		Total	999	17.5
	12–16[2]	Male	566	35.9
		Female	561	52.4
		Total	1127	43.9

1. Identified by parent and/or teacher.
2. Identified by parent and/or adolescent.

TABLE III

Unweighted prevalence (per 100) of depression, cross-classified according to informant, age and level of diagnostic certainty

Level of diagnostic certainty	*Age*	*Prevalence (per 100) cross-classified according to informant* *P*[1]	*T or A*[1]	*Both*[1]
High	6–11	0.3	0.3	0.0
	12–16	0.2	1.3	0.0
Medium	6–11	0.5	2.2	0.1
	12–16	1.0	6.4	0.2
Low	6–11	9.0	7.4	1.8
	12–16	5.0	30.3	8.5

1. P = parent only; T = teacher, for children aged 6–11; A = adolescent aged 12–16; Both = teacher or adolescent *and* parent.

TABLE IV

Percentage of subjects aged 6–16 having each external validating measure at each level of diagnostic certainty[1]

External validator	*Depressed status*	*Level of diagnostic certainty* *High*	*Medium*	*Low*
(a) Utilisation of mental health or social services	Depressed	21.5	12.7	9.3
	Non-depressed	5.8	5.6	3.7
(b) Comorbidity (≥ 1 OCHS disorder)	Depressed	95.8	63.2	34.9
	Non-depressed	12.9	11.6	4.6
(c) Poor school performance	Depressed	29.2	20.0	10.3
	Non-depressed	5.5	5.1	3.7
(d) Problems in getting along with others	Depressed	66.7	40.9	17.0
	Non-depressed	6.8	5.9	3.0
(e) Need for professional help	Depressed	33.3	31.4	15.0
	Non-depressed	6.3	5.9	2.2

1. All comparisons between depressed and non-depressed subjects are significant at $P < 0.001$.

subjects to have the validator. For depressed children, the highest percentages for all the validators were obtained in the high DC group and the lowest percentages in the low DC group, with percentages for the medium DC group falling in between.

Discussion

Estimates of prevalence rates

At high and medium levels of DC, our overall estimates of prevalence rates for depression in pre-adolescents of 0.6% and 2.7% fall within the range of estimates obtained in prior studies (i.e. 0.5–2.7%). The rate of 17.5% corresponding to low DC falls outside that range. In the adolescent age group, our prevalence estimates at all levels of DC (1.8%, 7.8% and 43.9%) fall between the low of 1.3% and the high of almost 50% found in previous studies. The overall prevalence of depression increased about threefold from pre-adolescence to adolescence; the same increase was reported by Rutter *et al* (1970).

We found that prevalence rates did not differ for male and female pre-adolescents. Previous studies have found either no effect of sex of child (Kashani *et al*, 1983; McCracken *et al*, 1989 (child-identified disorder)) or a higher prevalence of major depressive disorder in boys than in girls (Kashani & Simond, 1979; Anderson *et al*, 1987; McCracken *et al*, 1989 (parent-identified disorder)). For adolescents, we found a significant effect of sex of child only in the low DC group. In adult samples, women are consistently found to have higher rates of depression than men (Weissman & Klerman, 1977; Weissman *et al*, 1984). The findings for adolescents have not been consistent. Of the studies from Table I that examined sex of child as an effect, six found no effect of sex of child (Teri, 1982; Kaplan *et al*, 1984; Siegel & Griffin, 1984; Sullivan & Engin, 1986; Schoenbach *et al*, 1982; Wells *et al*, 1987), whereas four found a significantly higher rate of depression in females than in males (Reynolds & Coats, 1982, unpublished; Kaplan *et al*, 1987; Weinberg & Emslie, 1988; Kashani *et al*, 1987). In one study (Reynolds & Coats, 1982, unpublished) that used the BDI, females predominated over males in the categories of mild and moderate depression, but not in the category of severe depression. This is similar to our own finding of an effect of sex of child only for adolescents with the least severe depressive symptoms which suggests that perhaps female adolescents are more likely than males to report depressive symptoms, but no more likely than males to have a clinical syndrome of depression. This hypothesis will need to be tested in future studies.

Respondent disagreement

Our findings, consistent with the existing literature, showed poor agreement between responses from (a) parents and teachers and (b) parents and adolescents. By examining estimates of prevalence rates separately according to source, we found that teachers did identify pre-adolescent children as depressed, at lower, equal or greater rates than did parents, depending on the level of DC, which suggests that teachers have been underutilised as informants in past studies. Adolescents identified themselves as depressed about six times more often than parents identified them as depressed. Whether parents are unaware of their children's distress or adolescents are over-reporting symptoms, it will be important in future studies to examine the reasons for this discrepancy.

Diagnostic certainty or 'caseness'

Our division of 'high', 'medium' and 'low' DC was supported by our finding of increasing levels of the external validators as DC increased. It is also helpful to make comparisons with the existing literature. Comparison data are available only for comorbidity and utilisation of services. For example, high comorbidity rates of 79% (Anderson *et al*, 1987) and 100% (McCracken *et al*, 1989; Kashani *et al*, 1987) were found in the three studies that reported on comorbidity. In our sample, the comorbidity rate of 95.8% for high DC falls within the range found in these studies, whereas the rates of 63.2% and 34.9% for medium and low DC, respectively, do not.

With regard to utilisation of services, one study (McCracken *et al*, 1989) found that 25% of children identified as depressed by their parents were receiving treatment, while another study (Kashani *et al*, 1987) found that 47.1% of children currently depressed had sought professional help. Our utilisation rates for MH/SS are lower than these figures for all levels of DC, although the rate of 21.5% for the high DC group is comparable to the 25% rate (McCracken *et al*, 1989).

Considering all the evidence, we could conclude that the estimates of prevalence rates for a 'DSM–III-like' major depressive syndrome, obtained with high DC, are the most accurate. That is, the estimates are consistent with those in the literature, findings for comorbidity and utilisation of services for this group are most consistent with findings from previous studies, and there is the strongest evidence for impairment in this group. In the same vein, estimates of prevalence rates based on low DC are probably the least accurate. That is, the estimate of prevalence rates for pre-adolescents based on low DC falls outside the range reported in the literature, comorbidity and utilisation rates are much lower than those previously found, and there is the least evidence for impairment in this group. Finally, the accuracy of the estimates of prevalence rates based on medium DC probably falls between that of the high and low DC groups, given our findings that the estimates are consistent with those in the literature, but that the comorbidity and service utilisation rates for the group are lower than those previously reported.

Unfortunately, consistency between studies does not provide strong evidence for the accuracy of estimates of prevalence rates or any other findings, and it still remains true that estimates of prevalence rates have varied considerably from study to study and even within a study, depending on the definition of 'caseness'. The present study highlights the difficulty in deciding on the most useful criterion or criteria for 'caseness'. Kendell (1988, p. 375) stated that:

> "predictive validity is the best criterion available to us for validating the syndromes we recognise and for deciding where to draw the boundary between illness and temporary distress."

We recently completed a four-year follow-up of the OCHS sample and hope to examine the predictive validity of our diagnostic method in the near future.

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Season of Birth and Childhood Psychosis

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This paper reports a test of the hypothesis that winter birth is a risk factor for childhood psychosis. All psychotic children ($n = 208$) admitted to a day-treatment facility in Paris from 1960 through to 1986 were compared with 1040 controls matched by sex and year of birth. Risk ratio estimates were computed for each month, and a significant increase was observed for boys born in December. This association was stronger in some years than in others. The fact that there were no excesses in contiguous months detracts from the persuasiveness of this association.

During the past 25 years, much research effort has been devoted to the identification of risk factors for schizophrenia. One of the most consistent findings has been that those born during winter are disproportionately represented among adult schizophrenics. Boyd *et al* (1986) summarised the results of 30 studies conducted in 14 countries on different samples and with various methodologies. Despite possible statistical artefacts such as the use of inappropriate χ^2 statistics, or the role of phenomena labelled as incidence- and age-prevalence effects (Hare, 1975; Lewis & Griffin, 1981), which may have produced an overestimation in some studies, the validity of the association between birth during winter and the risk for schizophrenia seems to hold true. However, the magnitude of the effect is small. Boyd *et al* (1986) estimated the average excess risk among winter births to be about 10%. Some results suggest that winter-born patients exhibit distinctive characteristics compared with others: an earlier age of onset, a preponderance of females, a lighter genetic loading, and a better long-term prognosis.

Several possible explanations have been put forward, including vitamin deficiency, malnutrition during pregnancy, obstetrical and perinatal complications, foetal damage due to extreme temperatures, a seasonal pattern of conception among parents of schizophrenics, and viral infections (Bradbury & Miller, 1985). One of the most tenable aetiological factors is considered to be viral infection. Infections peak in the winter months and could affect newborns (Hare, 1986). However, there is still little research to support this hypothesis (Watson *et al*, 1984), and most of it has so far been confined to schizophrenia in adults.

If there really is an association between winter birth and the risk of schizophrenia, it is plausible that it might also be found for childhood schizophrenia and other related child psychiatric disorders. Genetic studies of infantile autism have shown that, in addition to hereditary components, environmental influences play an important role in the development of the disease (Folstein & Rutter, 1977). Furthermore, with regard to the aetiological role of viral infections in severe psychiatric conditions occurring in childhood, several studies have pointed to the higher incidence of infantile autism or autistic-like conditions following viral exposures or clinical illnesses, particularly rubella (Chess, 1971; Deykin & MacMahon 1979). Also, Nunn *et al* (1986) provided a rich clinical account suggesting again that late-onset childhood psychoses might be, at least in some instances, precipitated by various viral infections. It would therefore seem appropriate to examine the distribution of months of birth of children suffering from autism, neurodevelopmental disorders, and psychoses, in search of the same anomaly that was previously reported for schizophrenic adults.

Two studies have addressed the question of the relationship between season of birth and infantile autism (Bartlik, 1981; Konstantareas *et al*, 1986). Bartlik's study was conducted in North Carolina on a sample of 810 mildly to severely autistic children. A significant excess of births in March and August was found compared with the distribution of months of birth in the general population. When the sample was broken down according to the severity of the autistic features, this excess was not confirmed for the mild cases. For the more severely autistic children, the excess was found for the same two months, and a deficit was observed for October and November. The second study was carried out in Ontario on a sample of 179 autistic children referred for evaluation and treatment over 21 years (Konstantareas *et al*, 1986). The results indicated a significant excess of births among autistic patients during the spring and the summer, especially for March, May, and June. Further analyses led the authors to conclude that this phenomenon was most striking among the male, non-verbal, low-functioning subjects.

These two studies relied upon a comparison between cases selected from treatment centres and population data which were averaged straightforwardly across the time span of the studies. However, the distribution of births may vary appreciably from year to year in the same geographical area, and it has been suggested that a year-to-year approach should be used to calculate expected values for comparison with observed values (Hare *et al*, 1974; Lewis & Griffin, 1981).

There is also the matter of the appropriateness of using the general population as a control group. Information about births in the general population is usually available on a national or regional basis, but it is unclear whether or not these total population aggregates accurately reflect the referent population from which the cases are drawn. The use of mental health services is dependent upon many parameters unrelated to the disease and, even for severe conditions such as infantile autism, the completeness of case ascertainment in hospital-based studies should not be taken for granted (Rutter & Sandberg, 1985). Moreover, the information available focuses on the monthly distribution of live births and does not take into account the fact that some differential mortality may occur and later skew the distribution of the months of birth of that population. The existence of such an effect and its resulting influences have already been documented (Dalen, 1975; Hare, 1975). Another drawback of these studies lies in the reliance on χ^2 statistics for testing significance. Goodness-of-fit statistics test for any kind of departure from the null hypothesis of homogeneity of the distributions of months of birth. As previously suggested by research on adult schizophrenia (Shensky & Shur, 1982), cyclic trends are more accurately detected with tests of seasonality such as Roger's test (Roger, 1977). On the other hand, peaks may be ignored when comparisons are made by trimesters rather than by months. This practice is often used in order to gain statistical power (Boyd *et al*, 1986).

For the reasons discussed above, we decided to examine the possible association between month of birth and the later occurrence of childhood psychosis by adopting a case-control approach for the study design, as well as the more classic comparison with the general population.

Method

Site

The study was conducted in a child psychiatry facility which provides catchment-area services to one district of Paris. This is a publicly funded institution and access to the services is free of charge. Opened in 1960, the day-treatment hospital provides appropriate educational and psychological services for children suffering from severe psychiatric conditions. A full description of this institution and its clientele has been published elsewhere (Fombonne *et al*, 1988).

Selection of cases

From the 383 children admitted to the unit since 1960, all of those (54.8%) who had been diagnosed with childhood psychosis were included. The diagnostic information was extracted from each patient record, where it was readily available on an abstract sheet. The particular nosology used in this centre (Lebovici & Sadoun, 1968) did not allow for a distinction between subgroups of disorders within the psychotic category. No attempt was made to re-evaluate the clinical information to apply more precise diagnostic criteria because the records had no standardised format and the phenomenological descriptions were of unequal quality. The diagnosis itself was made by an experienced child psychiatrist and had been previously confirmed by a psychiatrist in the out-patient clinic. In two records, these two independent diagnostic assessments disagreed (emotional disorder versus childhood psychosis). It was decided to remove these two subjects from the initial sample because of the lack of a firm diagnosis. This resulted in a final sample of 208 cases for whom data on date of birth, date of admission, sex, and IQ were then collected. In six records data on IQ were missing. These six subjects were subsequently removed from further analyses. Information on place of birth was not collected, since in several cases it was inconsistently reported in the patients' records.

To assess the accuracy of data on date of birth, dates extracted from medical records were systematically compared with those appearing on the central register of the out-patient clinic. Only in three instances did the two dates differ, twice in the day of birth and once in the month. Errors in exposure were therefore minimal. There were 162 boys (78%) and 46 girls (22%), the sex ratio typically found in psychotic disorders in childhood. The subjects were born between 1948 and 1981, and their mean age at intake was 8.0 years (s.d. 1.9).

Selection of the controls

The controls were randomly selected from the medical records of children who had attended the out-patient clinic during the same period. For each case, five controls were selected. A ratio of five controls to one index case has desirable cost and power properties (Ury, 1975), and in this situation they were readily available. The controls were matched by sex and year of birth, and were selected within two years of admission of the cases in order to accommodate possible historical variations in the diagnostic process. When a subject met the criteria for sex and year of birth, the diagnosis and the reason for referral were examined on the abstract sheet (see above).

Subjects were included in the control group if they did not meet one of the following exclusion criteria: (a) psychotic state, (b) mental deficiency, (c) unspecified disorder labelled as 'other condition'. Mentally deficient children were excluded in light of previous reports on the existence of a relationship between IQ and month of birth (Knobloch & Pasamanick, 1958). The 'other condition' group was excluded because it reflected an unfinished diagnostic assessment or ambiguous cases which, in some instances, might later have been determined to be psychotic conditions.

A special case was made for those children referred to the centre before registration in the first year of public schools. These referrals result from a bureaucratic procedure that requires that some children who have not reached their sixth birthday by the end of calendar year undergo a psychological examination before enrolment. These children were generally classified in the 'no disorder' group, and their records bore a special mention which made them easily identifiable. Since by definition they represented a group of children primarily born in the first months of the year, these children were systematically excluded from the control group.

Only when a subject did not meet any of the above exclusion criteria were the day and month of birth disclosed and noted. In a few instances, whenever data about either diagnosis or date of birth were missing, the subject was no longer eligible to be a control. Finally, 1040 controls (810 boys, 230 girls) were selected according to this procedure, and the total size of the study sample was thus 1248.

General population data

Data on monthly distributions of live births for continental France from 1948 through to 1981 were obtained from the Institut National d'Etudes Démographiques. Such data were not available for each sex separately. For this entire period, the probability of being born in each month was computed as a weighted average of each year's probability during the study interval. The weights were the number of cases observed in the sample for each year.

Analysis

Data from the case and the control series were compared with data for the general population with a goodness-of-fit χ^2 test. An examination of seasonality was achieved for the cases and the controls by means of Roger's test. The direct comparison between the cases and the controls was carried out with a matched analysis conducted with the 208 sextuplets (one case, five controls). For each month of the year, the risk ratios were estimated by computing the exposure odds ratios according to the Mantel–Haenszel approach (Kleinbaum *et al*, 1982). An odds ratio that departs from unity means that the exposure, in our case the month of birth, differs for the cases and the controls. A conventional P value of 0.05 was retained to consider the results as statistically significant, although all the information conveyed by the 95% confidence intervals is used in order to draw inferences.

Results

Table I shows the distribution of births per month among the case and the control series, and the expected values under the null hypothesis of homogeneity with the general

TABLE I

	Cases			*General population*	*Controls*		
	Observed		*Expected*	*Probability of birth in each month*	*Observed*		*Expected*
	n	%	n	%	n	%	n
January	13	6.2	17.5	8.4	83	8.0	87.4
February	12	5.8	16.3	7.8	71	6.8	81.6
March	16	7.7	18.2	8.7	88	8.5	90.8
April	18	8.7	17.9	8.6	114	10.9	89.9
May	21	10.1	18.9	9.1	86	8.3	94.5
June	18	8.7	17.6	8.5	93	8.9	88.0
July	15	7.2	18.1	8.7	87	8.4	90.3
August	14	6.7	17.3	8.3	70	6.7	86.4
September	13	6.2	16.9	8.1	83	8.0	84.3
October	19	9.1	16.7	8.1	80	7.7	83.7
November	21	10.1	15.9	7.6	97	9.3	79.5
December	28	13.5	16.7	8.0	88	8.5	83.6
Total	208	100.0	208	100.0	1040	100.0	1040
Standard deviation		2.2				1.1	
Goodness of fit:							
by months	$\chi^2=14.3$, $P>0.10$				$\chi^2=16.7$, $P>0.10$		
by trimesters	$\chi^2=11.6$, $P<0.01$				$\chi^2=5.8$, $P>0.10$		
Roger's test	$R=0.6$, $P>0.50$				$R=1.95$, $P>0.25$		

population. Because of the smaller sample size, the standard deviation of the percentages for the cases is higher than for the controls. If we focus on birth rates that are one standard deviation below or above the mean percentage (8.3), a relative trough for February and a sharp peak for December are observed for the cases. The decrease for February parallels closely the numbers of the expected values and is also observed for the controls. On the contrary, for December, no parallel trend is found in the two control series. Compared with the cases, the controls exhibit a positive deviation in April which has no clear interpretation.

For the cases, the goodness-of-fit test is significant only when data are aggregated by trimesters, showing an excess of births in the last quarter of the year. No seasonal pattern emerges for the case series nor for the control group, as shown by the results of Roger's tests; that is, the months with relative excesses or troughs in birth rates do not tend to be contiguous. For the control group, which has a much larger sample size allowing more statistical power, neither goodness-of-fit test is significant. This may be regarded as a check of how well this control group represents the underlying referent population, since the monthly distribution of births of the clinic attenders is comparable with that of the general population.

Results of the direct comparisons between cases and controls are shown in Table II. For boys, the estimates of risk ratio are close to the null value except for the month of December, where a significant increase is found. In contrast to boys, girls exhibited no excess in December. Power to detect excesses among girls was low, however, because of the small sample size.

The male sample was then broken down according to IQ (IQ below or above 70), and the matched analysis was performed separately for low- and high-functioning subgroups. Table II shows that a higher increase in December births is found again for the low-IQ boys compared with the controls. This result was significant despite the small sample size of the subsample. None of the risk ratios computed in the high-functioning group was significant (data not shown), and the estimate for December was 1.8 (0.9–3.2) in that group.

TABLE II
Comparisons between cases and controls

	Boys (162 sextuplets)		*Girls (46 sextuplets)*		*Low-IQ boys (42 sextuplets)*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
January	0.4	(0.2–1.1)	2.4	(0.7–7.7)	0.2	(0.1–1.6)
February	1.1	(0.5–2.1)	0.3	(0.1–2.7)	1.1	(0.3–3.7)
March	0.8	(0.4–1.5)	1.4	(0.2–12.1)	0.7	(0.2–1.9)
April	0.9	(0.5–1.5)	0.4	(0.1–2.4)	0.7	(0.2–2.3)
May	1.0	(0.5–1.8)	2.5	(0.9–7.3)	1.2	(0.2–8.6)
June	1.2	(0.7–2.2)	0.4	(0.1–2.1)	1.9	(0.6–5.8)
July	1.0	(0.5–2.0)	0.4	(0.1–2.5)	2.5	(0.9–6.4)
August	1.1	(0.5–2.2)	0.8	(0.2–2.5)	1.9	(0.4–8.2)
September	0.7	(0.4–1.5)	0.9	(0.3–2.5)	—	—
October	0.9	(0.5–1.8)	2.2	(0.8–6.0)	0.4	(0.1–2.9)
November	1.1	(0.6–2.2)	1.1	(0.3–3.5)	0.6	(0.1–2.6)
December	1.9	(1.1–3.1)	1.0	(0.3–3.1)	2.9	(1.1–8.0)

OR = Odds ratio.
CI = confidence interval.

TABLE III
Relation between December births and psychosis according to different calendar periods (males only)

	No. of cases in the period	*No. of December births among cases*	*Odds ratio*	*95% CI*
1948–52	13	1	0.8	0.1–7.4
1953–57	17	4	2.3	0.6–8.3
1958–62	32	4	3.7	1.0–13.8
1963–67	36	7	6.0	2.0–18.2
1968–72	35	5	2.3	0.7–6.9
1973–77	23	1	1.3	0.1–1.8
1978–81	6	2	4.5	0.6–35.8

If birth in December is related to psychosis, the year of birth may also be important. In order to detect an effect of calendar time, we then stratified our data by five-year periods in order to ensure a sufficient number of cases per period. The resulting estimates of risk ratio are presented in Table III. The exposure–disease relationship is not uniform across the studied intervals, and it appears to be maximal for two periods (1958–62 and 1963–67), the risk ratio being significantly different from the null value for the latter period. The years 1966 and 1967 appeared to be responsible for this excess, since one-third of the cases born in these two consecutive years (4 out of 12) were born in December.

Because previous research reports on adult schizophrenia have examined the aetiological role of extreme temperatures (Bradbury & Miller, 1985), we looked at a possible relationship between December births and winter temperatures. For each year of the study period, data were obtained from the Météorologie Nationale (Observatoire du Parc Montsouris, Paris) about the average minimum daily temperatures for the winter periods (December through to February). During the study period, the average temperature of winters was 2.3 °C (s.d. = 1.3). Only in the year 1962 did the winter temperature fall below zero (−2.7 °C) and was far below the mean minus two standard deviations. However, only one patient was born in December 1962, and winters were not harsh in 1966 and 1967. Therefore, our data do not support any relationship between these two events.

Data on epidemics of infectious disease were not available for the most part of the study interval because monitoring systems on epidemics were largely ineffective and unreliable at that time. Thus, we could not test for any association between December births and infectious diseases.

Discussion

The distribution of births per month among the studied cases was found to differ from that of the general population, with an increase in the last trimester of the year. In addition, a more direct comparison led to the observation that the increase was limited to the month of December for boys only. This finding underscores the utility of using different control groups for comparisons, since the validity of a finding established with two different sets of controls is more convincing. The month of excess is similar to that found in studies on adult schizophrenics; however, it is different from those found in the two previous reports on autistic children and season of birth. Our results suggest that adult schizophrenia and childhood psychosis, although they are two distinct disorders, might possibly share a common risk factor, whether or not the underlying aetiological factor is indeed the same.

One difference between the North Carolina (Bartlik, 1981) and the Ontario (Konstantareas *et al*, 1986) studies and our own work lies in the different diagnostic criteria which were used. Explicit and reliable criteria were used in the North American studies, whereas a more imprecise diagnostic nomenclature was available for our study. Furthermore, most of the child psychiatrists at our centre rely upon the assessment of defence mechanisms, ego strength, and other psychoanalytical constructs in the diagnostic process rather than upon more explicit, phenomenological descriptions. As a consequence, they tend to overinclude patients in the 'psychosis' category. This has been documented in a prior study comparing the diagnostic assessments of three French-speaking psychiatric teams using the same nosology (Jongen *et al*, 1973). Therefore, misclassification with respect to diagnosis may have occurred in our data. However, although the magnitude of this misclassification remains unknown, it should be minimal since the condition of the children included in the sample was severe enough to warrant admission to a day-treatment hospital. Moreover, these errors, being independent of the birth date, can only have resulted in a bias towards the null value, leading to an underestimation of the association.

The strength of the association was found to be stronger in the subsample of low-functioning psychotic boys, despite its small sample size. This deserves two comments. First, misclassification is less likely to occur with low-functioning children, since they constitute a more 'pure' group of psychotic states. The fact that the association held true in this limited subgroup provides additional evidence of the validity of the finding. Second, it points to some possible mechanisms of the association. Because the association appeared to be stronger in the low-functioning group than in the high-functioning subgroup, it may be suggested that it is through a cognitive impairment that the factor involved acts in the causal chain. Similar results were obtained in the two studies already mentioned, and are consonant with existing knowledge on the role of cognitive processes and deficits in the aetiology of autistic conditions (Rutter, 1983). However, the relationship between season of birth, psychosis, and mental retardation needs to be further clarified with the study of a control group of non-psychotic mentally retarded children, which in the present study was not available. Such data are necessary to obtain unconfounded estimates of the association, and to assess the contribution of IQ and clinical status as independent risk factors.

Provided that the association is a causal one, it is to be stressed that the increase in the risk is minimal. Miettinen (1974) defined the "aetiological fraction" as the reduction in the number of cases which could be expected by removing the causal factor involved. If we derive from our data that a relative risk for infantile psychosis is in the range of two for boys born in December, it may be calculated that only 8% of male cases would be attributable to that factor (Schlesselman, 1982). This value, which is in the same range as that found for seasonal factors possibly involved in the aetiology of adult schizophrenia, points to the limited impact of these factors.

These data suggest that the influence of this factor may be unequal from year to year, although a much larger sample size would be needed to examine such time clustering more precisely. It is nonetheless suggestive of its epidemic nature. As in Konstantareas's study, the seasonal factor seems to be stronger for low-IQ boys, a result which suggests some brain damage occurring during the antenatal or early neonatal periods. For example, our finding that the increased risk in December is more pronounced in some years is compatible with the causal factor being pre-natal rubella, which in France peaks in the spring months. However, appropriate data to test this hypothesis are not available in France for the period in question.

The following comments on the validity of the reported association may also introduce another perspective on our results. Among the 12 monthly case-control comparisons, only the December one was significant. Had this result emerged in the context of a study with no prior hypotheses, it would have been tempting to invoke the purely statistical argument that there is a good chance of finding at least one significant result at $P=0.05$ when as many as 12 tests are carried out. However, the P value observed was quite low (0.018), and there was prior reason to suspect that there would be an increase during the winter. Our results support this hypothesis, albeit not decisively. The possibility that multiple testing led to some spurious significant results applies to other studies as well. For example, Bartlik (1981) carried out 24 χ^2 tests to analyse her data, and some of these may have been significant by chance.

Another comment relates to the rather arbitrary nature of the categorisation of 'exposure'. In order to be biologically plausible as a risk indicator, birth in one period of the year should not be limited *a priori* to one particular calendar month without producing similar effects in contiguous months. At least, moderate increases of the risk ratios should be perceptible in the preceding and following months. A smooth curve will be more convincing than a local peak. Our finding of an increased risk ratio for December male births only is disquieting inasmuch as it is followed by an abrupt trough in January. Similarly, the increased risks for March, June, and August births reported in Bartlik's and Konstantareas's studies are subject to caution.

The possible limitations suggest prudence in the interpretation of these studies. The reported excesses or deficits so far concern seven months of the calendar, with no consistent pattern across studies. Additional research is necessary to test further the association between season of birth and infantile autism or psychosis. These studies are relatively easy to conduct. Authors who have previously used psychiatric case registers or performed population-based studies should be able to shed light rapidly on this question. Studies thus far have failed to control for place of birth. Because season of birth appears to exert, at most, a minor influence, such lack of control could induce sufficient bias to mask true effects. Since potential causal explanations invoke an hypothesised environmental factor, which is likely to be non-uniformly geographically distributed, such information, as well as information about place of conception, pregnancy, and early post-natal life, is necessary for future studies. Another direction for research would be to obtain a large enough sample of females in order to examine possible sex differences in seasonality. Finally, similar to studies in adult schizophrenics (Machon *et al*, 1983; Bradbury & Miller, 1985), data on genetic background would assist in the study of interactions with environmental variables and provide clues to possible causal mechanisms.

Note

A recently published study (Tanoue *et al*, 1988) provides some evidence of a relationship between birth in the second trimester and an increase of the prevalence rate of autism in some, but not all, birth cohorts of Japanese children.

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Season of Birth in Alzheimer's Disease

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Variation in quarter of birth was examined in patients with a clinical diagnosis of AD. There was a significant excess of first-quarter births among AD patients as compared with the expected birth rates derived from an age-matched census sample. This finding was due entirely to the significant excess of first-quarter births in AD patients without a family history of dementia. No seasonal variation was found in the birth dates of other clinical groups.

Alzheimer's disease (AD) is a progressive neurodegenerative disorder of insidious onset. The cause is unknown but evidence for the genetic basis of AD has been accumulating for some time (Holland, 1987). However, a search for environmental factors of aetiological significance has been made and it has been claimed that AD is associated with advanced maternal age (Cohen *et al*, 1982); a past history of head injury, often decades prior to the onset of the dementia (Heyman *et al*, 1984; Mortimor *et al*, 1985); a past history of thyroid disease in women (Heyman *et al*, 1984); and chronic exposure to high levels of aluminium in drinking water (Vogt, 1986). In addition, geographical clustering of new cases has been described (Whalley & Holloway, 1985) and a number of infectious agents have been implicated (Ball, 1982; Prusinier, 1984; Renvoize & Hambling, 1984).

Seasonal variations in births have been demonstrated for a number of disorders, including Down's syndrome and other forms of mental retardation (Edwards, 1961; Dalen, 1975), schizophrenia, manic–depressive psychosis, anxiety neurosis and personality disorder (reviewed by Dalen, 1975). Many of these studies have been criticised and their findings challenged, but the association between schizophrenia and birth in winter, in the northern hemisphere, remains robust (Hare *et al*, 1974; Bradbury & Miller, 1985; Boyd *et al*, 1986). This observation has been cited as evidence for the operation of environmental factors in the aetiology of schizophrenia (Hare, 1986). The assumption is made that birth in winter exposes the individual to some environmental hazards whose effect may predispose to schizophrenia in later life. There is some evidence that the 'winter-birth seasonality' effect is greater in years directly following those with high levels of infectious diseases (Watson *et al*, 1984). Some studies have shown that the effect is greater in schizophrenics with a low genetic risk for the disease (Kinney & Jacobsen, 1978; Sensky & Shur, 1982) and in schizophrenics with cerebral atrophy (Zipursky & Schulz, 1987; Degreef *et al*, 1988).

A recent study of idiopathic Parkinson's disease, while concerned chiefly with variation in year of birth, revealed an excess of Parkinsonian births in May and a paucity in July (Mattock *et al*, 1988). Given the range of disorders reputed to show seasonal birth variation we decided to investigate whether a cyclical distribution of births was also to be found in patients suffering from AD.

Method

Month and year of birth were identified for all patients of Caucasian origin from three sources:

(a) consecutive referrals to the Maudsley Hospital Memory Clinic between its inception in May 1984 and December 1987
(b) consecutive admissions to the psychogeriatric day hospital (Felix Post Unit) and in-patient beds (Gresham House) between October 1982 and September 1985
(c) patients living in the Camberwell Health District (aged over 65) who were enrolled in a study of the natural history of AD.

Information concerning family history of dementia was obtained from the spouses or children of patients from sources (a) and (c). A 'positive' family history of dementia was recorded if at least one parent or sibling had suffered from global and progressive cognitive impairment in the absence of a previous history of stroke.

Patients from these sources were then subdivided by diagnosis into the following three groups: patients fulfilling the NINCDS–ADRDA clinical diagnostic criteria for 'probable' AD (McKhann *et al*, 1984); those with other organic psychoses (chiefly multi-infarct dementia); and those with functional psychiatric disorders (depression and paraphrenia). All the patients in the AD group had undergone a full battery of screening investigations, including CT brain scan, to exclude any secondary or reversible dementias (Philpot and Levy, 1987).

Observed quarterly birth rates were compared by χ^2 evaluation with 'expected' rates derived from published census data. In the UK, births were not recorded by month until 1938. Before that date only a quarter of birth *registration* is available. However, during the 1971 census,

TABLE I
Comparison of quarter of birth of each diagnostic group with expected quarterly variation derived from age-matched general population census data of month and year of birth (1971 1% sample)

	Quarter of birth				*Total births*	χ^2 *(d.f. = 3)*	*P*
	1st	*2nd*	*3rd*	*4th*			
Alzheimer's disease							
Observed births	75	52	60	52	239	6.35	<0.1 >0.05
Expected births	59.1	60.9	60.3	58.6	238.9		
Observed as percentage of expected	127	85	100	89	100		
Other organic psychoses							
Observed births	23	17	24	25	89	2.12	>0.1
Expected births	22.0	22.8	22.5	21.7	89		
Observed as percentage of expected	105	75	107	115	100		
Functional							
Observed births	47	45	55	41	188	1.97	>0.1
Expected births	46.6	48.5	47.3	45.6	188		
Observed as percentage of expected	101	93	116	90	100		

month and year of birth were recorded for a 1% sample of the population (Office of Population Censuses and Surveys, DT 1643). We determined the 'age' structure of our patient sample by stratifying it by decade of birth from 1876 onwards and consequently adjusted the age structure of the census sample to match. The proportion of the population born in each quarter was then used to calculate the 'expected' births per quarter (details of method available on request).

In addition to the simple χ^2 comparisons, we applied Roger's method for testing the significance of cyclic trends (Roger, 1977) and Edwards's method for determining the peak quarter of birth (Edwards, 1961).

Results

The clinical notes of 534 patients compiled from the three sources were studied. There were 204 patients from the Memory Clinic sample, 253 admitted to the psychogeriatric service and 77 in the natural history study. Date of birth was not known in 18 cases and these were excluded from further analysis. There were 239 patients with AD, 89 with other organic psychoses and 188 with functional psychiatric illnesses.

Table I shows the numbers of observed and expected births per quarter for each diagnostic group. The first quarter excess for AD births approaches significance, but there is no significant seasonal variation for the other diagnostic groups.

Table II shows a comparison of each individual quarter with the remaining quarters – a procedure used in many previous studies of seasonality (e.g. Hare *et al*, 1974). Using this method a statistically significant excess of first-quarter births emerges ($P<0.02$).

Family history data was available for 193 of the AD patients, and Table III shows the variation of the quarter of birth for those with and those without a family history of dementia. A significant first-quarter excess of births of those *without* a family history is revealed ($P<0.01$). This result is almost entirely due to excess births in January and February. The tendency for there to be a paucity of first-quarter births in those *with* a family history of dementia does not reach significance ($P>0.1$). When the two groups are compared directly, the excess of first-quarter births in those without a positive family history, as compared with births in the remaining three quarters, remains highly significant ($\chi^2=11.6$, d.f. = 1, $P<0.001$).

Table IV shows the results of applying Roger's and Edwards's tests to the seasonal birth distribution of AD patients. These calculations are not dependent on population controls and confirm that AD patients with 'low' genetic risk of dementia are more likely to be born

TABLE II
Chi-square analysis of AD patient birth-dates comparing individual quarters with all remaining quarters

Quarter of birth	*Observed births*	*Expected births*	*Comparison of individual quarter with all remaining quarters*	
			χ^2 *(d.f. = 1)*	*P*
January–March	75	59.1	5.67	<0.02
April–June	52	60.9	1.79	>0.1
July–September	60	60.3	0.003	>0.9
October–December	52	58.6	1.83	>0.1

TABLE III
Variation of quarter of birth for AD patients with (FH+) and without (FH−) a family history of dementia

	Quarter of birth				*Total*	χ^2 (*d.f.* = 3)	*P*
	1st	*2nd*	*3rd*	*4th*			
AD, FH+							
Observed births	12	20	21	21	74	3.04	>0.1
Expected births	18.4	18.9	18.7	18.1	74.1		
Observed as percentage of expected	65	106	112	116	100		
AD, FH−							
Observed births	47	24	28	20	119	14.85	<0.01
Expected births	29.4	30.4	30.0	29.1	118.9		
Observed as percentage of expected	160	79	93	68	100		

TABLE IV
Comparison of cyclical trends for births of AD patients with and without family history of dementia and for general population

Group	*Number*	*Significance of cyclical trend*[2]	*Peak quarter or month*[3]
Low genetic risk	119	$P<0.05$	Early 1st
High genetic risk	74	$P<0.4$	Early 3rd
General population 1971 1% sample	215 417[1]	$P<0.0005$	May

1. Population born in England and Wales between 1876 and 1935 and living in 1971.
2. Calculated by Roger's method.
3. Calculated by Edwards's method.

in the first quarter ($P<0.05$). The significance and peak of the monthly variation of the general population born between 1876 and 1935 and enumerated during the 1971 1% census sample are shown for comparison.

Discussion

The results of the present study indicate that there is a significant excess of first-quarter births among subjects with AD who have no family history of dementia. The inverse of this (i.e. a relative under-representation of first-quarter births) in those with a family history has thus weakened the cyclical trend in the AD group as a whole.

The observation presented here points towards a potentially fruitful area for the future investigation of early environmental influences in the aetiology of AD. There are, however, several methodological problems associated with this study in particular and birth seasonality research in general.

Experimental subjects

The current study employed patients derived from three diverse sources. The Memory Clinic patients were those referred for specialist assessment of their cognitive problems from the south-east of England. The patients admitted to the psychogeriatric service and those in the natural history study were those over the age of 65 referred from within the hospital catchment area. In addition, it was not possible to control for important variables such as social class, place of birth, birth order or other environmental exposure.

A second problem, and one which affects any clinical study of AD, concerns accuracy of diagnosis. The correlation between clinical and neuropathological diagnosis is often poor (Nott & Fleminger, 1975; Homer *et al*, 1988). However, the NINCDS-ADRDA criteria for 'probable' AD (McKhann *et al*, 1984) applied in this study have recently been shown to correspond with post-mortem diagnosis in 80–90% of cases (Tierney *et al*, 1988).

Controls

No clinical control group was used in this study in view of the possibility of introducing a confounding factor resulting from the reported seasonal variation of other psychiatric illnesses such as manic-depressive psychosis, which is common in the elderly (Hare, 1975).

The use of general-population birth statistics to derive expected figures for quarterly variation poses a particular problem of accuracy when dealing with UK data prior to 1938. Before then, registration date rather than birth date was recorded. An individual born in May, for example, might not have been registered until August and therefore be allocated to a different quarter. However, birth statistics *per se* may not be the best source of 'control' information when studying a group of elderly patients. Those who live long enough to develop dementia represent a survivor group. Reports of seasonal fluctuations in a whole range of disorders, including infective and neoplastic disease, affecting individuals throughout life are reviewed by Dalen (1975). Thus the use of the 1971 1% sample data, where the birth dates of 'survivors' were recorded, provides the most reliable basis for the calculation of expected frequencies.

Statistical analysis and sample size

Although χ^2 analysis is simple and has been used in many other studies, its use may not be entirely appropriate as it may not be sensitive to cyclical trends. The more sophisticated statistical techniques of Edwards (1961) and Roger (1977) used here have also been advocated by others (Sensky & Shur, 1982), but Bradbury & Miller (1985) have proposed the use of the even more rigorous techniques of time-series analysis.

Perhaps the major limitation of the current study lies in the small size of the sample. The compilation of a large sample of carefully diagnosed cases presents a considerable problem.

Family history

Of the 193 AD patients for whom the information was available, 74 (38%) had at least one first-degree relative with dementia. This figure accords with those found in other studies (Heston *et al*, 1981; Holland, 1987). Possession of a similarly affected relative can only be a rough guide to increased genetic 'loading', as more than one sporadic case may conceivably occur within the same family, particularly if relatives are long-lived or numerous.

Age-incidence and age-prevalence effects

In any particular calendar year an individual born in January is almost one year older than an individual born in December. For any condition whose incidences or prevalence increases with age, such as AD, the older January-born subjects will be at greater risk from the disease than the younger December-born subjects. January-born AD patients may be more severely affected than December-born patients by virtue of having had the disease longer: they may come to medical attention sooner.

However, if these effects operated in AD one would expect a first-quarter excess in all subtypes of AD patients and not only those without a positive family history. In addition, a first-quarter excess would be found in the group with other organic psychoses, which also increase in prevalence with age.

Explanations for the winter-birth effect

In determining the possible significance of the observations reported here, we have borrowed a number of explanations which have been proposed to account for the winter-birth effect in schizophrenia (Bradbury & Miller, 1985).

The *procreational habits hypothesis* proposes that the parents of the affected individual conceive more frequently in the spring months, thereby producing a first-quarter birth excess. Without the luxury of a long-term prospective study, it would be difficult to investigate the habits of the parents of AD patients, although it should be possible to test the hypothesis by examining the seasonal distribution of births in unaffected siblings.

The *amplified deviation hypothesis* proposes that the factors responsible for the seasonal distribution of births in the general population also operate in the affected group but to a greater extent. However, we have compared the birth distribution of our patients with figures derived from the general population, whose births have a different seasonal distribution.

The *genetic fitness hypothesis* proposes that the disease genotype confers a robustness which enables the individual to survive birth in winter or premature death from other diseases. There is some evidence that patients with AD are more fit than age-matched controls (Wolf-Klein *et al*, 1988), but this is probably an artifact arising from the method of research diagnosis, which involves the exclusion of patients with medical or psychiatric disorders associated with other forms of dementia.

The *harmful effects hypothesis* assumes that birth in winter is more hazardous and proposes that individuals are damaged, in some way, by contact with adverse environmental factors such as extremes of temperature, nutritional deficiencies, infectious agents or an increased rate of obstetric complications. Infections such as diphtheria, pneumonia and influenza were found to be particularly associated with increased winter births of 'process' schizophrenics

(Watson *et al*, 1984), and individuals born in years of influenza pandemics appear to have an increased risk of developing Parkinson's disease in later life (Mattock *et al*, 1988).

In view of the variety of conditions which show a seasonal distribution of patients' births it must not be assumed that this finding is necessarily of aetiological significance, but clearly, in relation to Alzheimer's disease, larger studies – ideally of cases verified post mortem – need to be carried out before more definite conclusions can be made.

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The Predictive Value of the Dexamethasone Suppression Test

A Placebo-Controlled Study

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We evaluated the dexamethasone suppression test (DST) as a predictor of response to drugs and placebo in 105 patients, in a large double-blind placebo-controlled out-patient trial to determine the efficacy of paroxetine HCl, a selective serotonin reuptake inhibitor, compared with that of imipramine HCl and placebo. The presence of a positive or negative DST did not predict response to either paroxetine or imipramine. However, a positive DST predicted a poorer response to placebo: only 3 out of 18 patients who showed DST non-suppression responded to placebo, as opposed to 11 out of 21 who exhibited DST suppression ($P<0.05$). A positive DST was associated with a 61% response to drugs and a 16% response to placebo. This finding suggests that the presence of a positive DST implies the need for active somatic treatment.

Over the past decade the dexamethasone suppression test (DST) has been widely employed as a clinical and research tool in evaluating overactivity of the hypothalamic–pituitary–adrenal axis in depressed patients (Arana & Baldessarini, 1987). A recent review of the literature noted over 261 reports on the DST between 1980 and 1983, making it the single most extensively studied test in psychiatry (Baldessarini & Arana, 1985). Despite varying methodologies used to categorise depression, inadequate suppression of cortisol following overnight dexamethasone administration has been demonstrated in 25–60% of patients with primary affective disorder (Carroll *et al*, 1981; Carroll, 1985).

The majority of the reports on the DST are concerned with issues of diagnostic sensitivity and specificity. It would be useful to know whether, in addition to supporting depressive diagnosis, the DST has any utility in predicting short-term antidepressant response. Many reviews of the literature evaluating the predictive ability of the DST with respect to varied somatic treatments have yielded mixed results (Arana *et al*, 1985; Arana & Baldessarini, 1987; Braddock, 1986). The majority of the studies done to date have not examined the DST within the context of a placebo-controlled drugs trial. It is the purpose of this paper to evaluate the DST as a predictor of response to both drugs and placebo in out-patients with major depression.

Method

Over a 21-month period from May 1985 to February 1987, our group conducted a large antidepressant trial in an attempt to evaluate the efficacy of the selective serotonin reuptake inhibitor, paroxetine HCl, compared with that of imipramine HCl and placebo. Overall, 137 patients with major depressive disorder gave voluntary informed consent to participate in the trial. All patients who gave consent were treated as out-patients at the Foundation for Depression–Manic Depression. All patients involved in the trial met DSM–III criteria for major depression, were 18 years of age or older, and had a minimum score of 18 on the first 17 items of the 21-item Hamilton depression scale (Hamilton, 1967).

If the patient fulfilled the above criteria, he or she was then placed on single-blind placebo over a 4–10 day period. At the outset of this period, as many individuals as possible were given 1 mg of dexamethasone to take at 11 p.m. These individuals returned the next day for morning (approximately 8–9 a.m.) and afternoon (approximately 4 p.m.) plasma cortisol to be drawn. All patients who participated in the trial were free from active medical illness, endocrinopathy, and current substance abuse.

Following the one-week single-blind placebo period, all patients were reassessed with numerous clinical scales that they had received at initial screening, including the Hamilton depression scale, Montgomery–Asberg depression scale (Montgomery & Asberg, 1979), CGI (clinical global improvement) scale, Raskin depression scale (Guy, 1976), and the Beck Depression Inventory (Beck & Beamsderfer, 1974). In addition, a global improvement scale was completed by both the patient and physician at each visit (called patient and MD global scale respectively). This scale rated improvement or worsening from baseline on a 1–3 point scale (+1 to +3 indicating mild, much or very much improved, −1 to −3 indicating mild, much, or very much worse, and 0 indicating no change from baseline). The patient was also rated on a 13-item endogenous depression scale that was abstracted from the SADS-C (Endicott & Spitzer, 1978), and it was determined whether the patient met Research Diagnostic Criteria for definite endogenous depression (Spitzer *et al*, 1978). If the patient's Hamilton score remained above 18 and did not drop more than 20% below its value prior to the single-blind placebo phase, the patient was then able to enter the double-blind phase of the trial. Overall, 122 patients were eligible to enter the double-blind phase.

In the double-blind phase six-week trial the patient received either paroxetine HCl (in dose ranges of 10–50 mg/day), imipramine HCl (in dose ranges of 65–275 mg/day) or placebo. Randomisation to either drug or placebo was based on an attempt to evaluate drug efficacy; the randomisation was not related to DST value.

All patients who entered the double-blind trial were seen weekly, and formally rated with the above scales at weeks 1, 2, 3, 4 and 6. At the end of the six-week period, or final endpoint analysis, a determination of response to treatment was made. A response to treatment was arbitrarily defined as a 50% or greater reduction in both Hamilton score from baseline and Beck score from baseline, or a final CGI score of 1 or 2 (much improved or very much improved) compared with baseline.

For the purposes of this analysis, we present DST data on the paroxetine and imipramine groups both separately and in combination. The reason for this is that, although there is reported efficacy for paroxetine in depressive illness (Borop *et al*, 1982; Lund-Laursen *et al*, 1985), and although paroxetine was as effective as imipramine in depressive illness in a large multi-centre study of which the present trial formed part, in our particular site, there were trends towards patients showing greater improvement on imipramine than on paroxetine (both superior to placebo), an improvement that in some cases approached statistical significance. The DST as a predictor of response in patients is compared for both drugs and placebo.

A positive DST was defined as a morning or afternoon plasma cortisol value greater than or equal to 5 μg/dl. Cortisol determinations were made by commercial radioimmunoassay (RIA) kit. The intra-assay coefficient of variation was between 7% and 8%. Overall, our group was able to obtain DST data on 105 of the 122 patients who entered the double-blind trial.

The 105 patients in this evaluation had an average age of 44.6 years. There were 67 males and 38 females (the main reason for the sex differential was that for the first 9 months of the trial we were not allowed to enter women of child-bearing potential). The average age of onset of the patients' first depressive episode was 29.8 and the average length of the current episode was 5.6 months. There was no difference in the above parameters for these patients compared with either the 17 other patients in the double-blind trial for whom we were unable to obtain a DST, or the 15 patients who signed consent for the trial but did not reach the double-blind stage.

Results

In Table I the demographic characteristics and response rates for the three treatment groups are examined. There was no difference in any of the demographic characteristics (age, duration of illness, length of current depressive episode, or sex ratio) among patients randomised to any of the three treatment groups. In addition, as has been previously reported, there was no difference in initial severity of depressive illness as measured by the above-mentioned scales among the three groups. Overall, when the code was broken, for the patients for whom a DST was obtained, 17 out of 34 patients had responded to

TABLE I

Response to paroxetine, imipramine and placebo

	Paroxetine (n=34)	*Imipramine (n=32)*	*Placebo (n=39)*	*Probability*
Demographic characteristics				
Age	44.3	47.7	42.2	$P=0.68$
M/F	21/13	22/10	24/15	$\chi^2=1.02$, d.f. 2, $P>0.7$
Age at onset	31.1	30.3	28.6	$P=0.61$
Length of current episode (months)	6.2	5.5	5.1	$P=0.71$
Treatment characteristics				
Responders	17(50%)	21(66%)	14(36%)	$\chi^2=6.22$, d.f. 2, $P=0.04$[1]
Improvement (decrease in score from baseline)				
Hamilton: %	41.71%[2]	60.19%[2]	16.95%	$P=0.0001$
Beck: %	46.30%[2]	60.10%[2]	16.60%	$P=0.0001$
Raskin	2.88	4.69[3]	1.59	$P=0.0002$
CGI	1.06	1.88[3]	0.54	$P=0.0001$
Montgomery–Asberg: %	41.00%[2]	55.10%[2]	17.30%	$P=0.0002$
MD global	1.35[2]	1.81[2]	0.33	$P=0.0001$
Patient global	1.24[2]	1.78[2]	0.21	$P=0.0001$

1. Imipramine superior to placebo.
2. Paroxetine and imipramine statistically better than placebo.
3. Imipramine statistically better than paroxetine and placebo.

Note that changes from baseline for Hamilton, Beck, and Montgomery–Asberg scales are expressed as percentage change. For the other scales the change is expressed in absolute values.

TABLE II

Frequency of positive DSTs for the three treatment groups and response to treatment

Treatment group	*Positive DSTs*	*Negative DSTs*	*Positive DST responders*	*Negative DST responders*	*Probability*[1]
Paroxetine ($n=34$)	12 (35%)	22 (65%)	6/12 (50%)	11/22 (50%)	$P=1.00$
Imipramine ($n=32$)	16 (50%)	16 (50%)	11/16 (69%)	10/16 (63%)	$P>0.8$
Total drug ($n=66$) paroxetine + imipramine	28 (42%)	38 (58%)	17/28 (61%)	21/38 (55%)	$P>0.9$
Placebo ($n=39$)	18 (46%)	21 (54%)	3/18 (16%)	11/21 (52%)	$P<0.05$[2]

1. Probability refers to difference between positive and negative DST responders.
2. Statistically significant.

paroxetine, 21 out of 32 had responded to imipramine and 14 out of 39 had responded to placebo, according to our previously mentioned criteria. This rate was approximately the same if one considered the whole sample. If one examines improvement from baseline scores, both drug treatment groups were better than placebo. For some measurements (i.e. Raskin and CGI), patients showed greater improvement on imipramine than on paroxetine.

In Table II the positive DST rate for the three treatment groups and the response to treatment for the three treatment groups based on DST value are examined. The positive DST rate was 35% (12 out of 34) for the paroxetine group, 50% (16 out of 32) for the imipramine group, and 46% (18 out of 39) for the placebo group. This difference was not statistically significant ($\chi^2=1.55$, d.f. 2, $P<0.3$).

With respect to response to treatment for the three treatment groups based on DST value (Table II), for the two drug-treated groups, the presence of a positive or negative DST did not predict response to either imipramine or paroxetine. Overall, 17 out of 28 (61%) patients with a positive DST responded to either drug compared with 21 out of 38 (55%) patients with a negative DST. This difference was not statistically significant ($\chi^2=0.20$, d.f. 1, $P>0.9$). However, only 3 out of 18 (16%) of those with a positive DST responded to placebo compared with 11 out of 21 (52%) with a negative DST ($\chi^2=3.91$, d.f. 1, $P<0.05$). Stated another way, a positive DST yielded a 61% response rate to drugs (17 out of 28 of those with a positive DST responding to either paroxetine or imipramine) but only a 16% (3 out of 18) response to placebo ($\chi^2=6.96$, d.f. 1, $P<0.01$).

In order to evaluate whether DST value alone was primarily responsible for the placebo response, we attempted to evaluate the clinical characteristics of the 105 patients by dividing them into those who had an initial positive DST and those who did not. Overall 46 of the 105 patients had a positive DST, as characterised by having a morning or afternoon cortisol value equal to or greater than 5 μg/dl. As can be seen from Table III, those with a positive DST tended to have a more severe depressive illness, as characterised by higher scores on most scales, which in some cases reached statistical significance (CGI scale, and Montgomery–Asberg scale). The patients with a positive DST tended to have statistically greater endogenous features and were more likely to meet RDC criteria for definite endogenous depression than were those with a negative DST.

TABLE III

Characteristics of patients with positive and negative DSTs

	Positive DSTs[2] *(n=46)*	*Negative DSTs (n=59)*	*Probability*[3]
Initial score			
Hamilton	28.22	26.36	$P=0.069$
Beck	28.65	27.25	$P=0.051$
Raskin	11.22	10.93	$P=0.30$
CGI	4.65	4.37	$P=0.033$[1]
Montgomery–Asberg	33.89	31.66	$P=0.035$[1]
Endogenous symptoms	37.07	31.22	$P<0.0001$[1]
RDC definite endogenous depression	34/46 (74%)	18/59 (31%)	$\chi^2=19.48$, d.f. 1, $P<0.0001$[1]

1. Statistically significant.
2. Defined as either morning or afternoon plasma cortisol ≥ 5 μg/dl.
3. Statistics done on unpaired *t*-tests.

TABLE IV

Clinical characteristics of patients randomised to placebo

	Placebo responders (n=14)	*Placebo non-responders (n=25)*	*Probability*[2]
Initial score			
Hamilton	25.86	28.00	$P=0.15$
Beck	27.07	27.56	$P=0.66$
Raskin	11.14	11.40	$P=0.57$
CGI	4.21	4.68	$P=0.04$[1]
Montgomery–Asberg	31.07	33.28	$P=0.25$
Endogenous symptoms	31.74	34.96	$P=0.19$
RDC definite endogenous depression	6/14 (43%)	14/25 (56%)	$\chi^2=0.62$, d.f. 1, $P=0.65$

1. Statistically significant.
2. Statistics done on unpaired *t-tests*.

In Table IV the clinical characteristics of the 39 patients randomised to placebo are broken down into responders and non-responders. For all measures except initial CGI, there was no statistically significant difference between placebo responders and non-responders with respect to initial severity of pathology as measured by the scales that we used. Most important, the degree of endogenous symptoms or the diagnosis of endogenous depression did not differentiate between placebo responders and placebo non-responders.

Discussion

As noted in several review articles (Arana *et al*, 1985; APA Task Force on Laboratory Tests, 1987), when one combines data from 20 studies examining the predictive value of the DST with respect to antidepressant or other somatic treatment, there is no difference in response rate between those who started with a positive DST and those who began with a negative DST, with the overall response rate to treatment noted as 70%. However, a review of some of these frequently quoted studies on an individual basis shows contradictory results at best. Two initial studies (McLeod *et al*, 1970; McLeod, 1972) and a more recent study (Ames *et al*, 1984) suggested that the presence of positive DST augured a poor response to varied antidepressant treatment. Other retrospective work suggested that patients with a positive DST have a high rate of response to somatic treatment whereas individuals with a negative DST have a low rate of response to such treatment (Brown *et al*, 1979; Brown & Shuey, 1980; Greden *et al*, 1981).

In addition, reviews of prospective controlled studies (individuals given the same treatment with investigators blind to DST results) have also yielded mixed results. Amsterdam *et al* (1983), in giving desipramine to 40 depressed out-patients, reported greater improvement in DST suppressors compared with non-suppressors which just missed statistical significance. Janicak *et al* (1987) noted that DST non-suppressors had a statistically poorer response to phenelzine as opposed to DST suppressors. In contrast, Nelson *et al* (1982) and Coryell (1982) suggested that patients with a positive DST had a better response to antidepressants (imipramine and amitriptyline) and ECT respectively. Finally, studies by Green & Kane (1983), Young *et al* (1982), Peselow *et al* (1985), and Peselow *et al* (1986*a*) suggested that the presence or absence of a positive DST did not preferentially predict response to a number of antidepressants (desipramine, nortriptyline, imipramine, or amitriptyline).

The inability of the DST to predict response to paroxetine in the present study is interesting and is opposed to the finding of Brown *et al* (1985), who noted that patients with a positive DST had a poorer response to an equally selective serotoninergic agent, fluvoxamine. Other studies suggesting that the DST predicted specific response to specific antidepressants have yielded contradictory results (Brown & Qualls, 1981; Beckmann *et al*, 1984; Peselow *et al*, 1986*b*).

The above studies, unlike that described here, did not have a placebo control, and thus do not permit the rate of true drug response to be distinguished from that of spontaneous remission. To date there have been six reported studies that have examined this question. An in-patient study by Peselow *et al* (1986*b*), combining two new drug v. placebo trials, noted that while a positive or negative DST did not predict a response to drugs, the presence of a positive DST predicted a poorer response to placebo. A recent study by Zammitt *et al* (1988) noted that placebo responders tended to have negative DSTs. Out-patient studies combining either data from several sites (Brown *et al*, 1987) or combining several different out-patient drug v. placebo studies (Peselow *et al*, 1988) also noted that a positive DST yielded a poor response to placebo, with no preferential response to drugs. However, out-patient studies by Georgatas *et al* (1986) and Kahn *et al* (1988) noted that a positive or negative DST did not predict a response to drugs or placebo.

Since major depression is a heterogeneous entity and since there are numerous treatments for it (Kovacs *et al*, 1981; Weissman *et al*, 1981), the presence of an objective parameter to monitor clinical course would be useful to the treating psychiatrist. If the DST were useful in predicting which form of treatment, i.e. pharmacotherapy, psychotherapy, cognitive therapy, etc., should be used for depressive illness, clinical judgement could be aided by an objective parameter so as to give the best possible outcome for the patient. A study by Rush (1984) noted that patients with a positive DST had a poorer response to cognitive therapy than had those with a negative DST.

In the present study the individuals with a positive DST had more severe depressive symptoms and greater endogenous features than those with negative DSTs (Table III), in concordance with what has previously been reported (Carroll *et al*, 1981). From this it can be suggested that the DST is not as much responsible for the differentiation between drug and placebo response as is the difference in severity and endogenous features. In the present study this was not the case, as there was no difference between eventual placebo responders and non-responders with respect to either initial severity, as measured by the scales we employed, or degree of endogenous symptoms (Table IV). However, in order better to evaluate this contention, future double-blind trials are needed that would randomise patients to antidepressant or placebo (or other treatments) primarily on the basis of the presence of a positive or negative DST, with severity of illness and presence of melancholic features (or diagnosis of melancholia) considered in setting up balanced subgroups. This would not only allow us to assess the predictive value of the DST, but would also help us to answer the question whether the DST or severity of illness, or the presence of melancholia, or a combination of all three, are related to treatment response.

In summary, in this large out-patient sample, it appeared that while the DST did not predict response to either drug treatment, the presence of a positive DST, as opposed to a negative DST, predicted a poorer response to placebo. The finding, if confirmed, would suggest a possible clinical utility for the test, in that the presence of a positive test would suggest little likelihood of recovery without active pharmacological treatment, and would suggest the need for somatic therapy.

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A Comparison of Early-Onset and Late-Onset Depressive Illness in the Elderly

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Elderly patients with early-onset and late-onset depressive illness presenting to psychiatrists for treatment were compared for social, demographic, and clinical measures. For most factors measured no statistically significant differences were found. In the early-onset cases, patients were significantly more severely depressed. There was some evidence for the hypotheses that family history is less important and biological factors more important in late-onset depression. It is suggested that the latter hypothesis should be tested by a range of the newer neuroanatomical and neurophysiological laboratory investigations. The findings indicate that neuroticism is an important underlying factor in both early-onset and late-onset depression in the elderly.

Depressive illness is common in the elderly and has recently become the focus of much research. Its prognosis is relatively poor and it is characterised by frequent and prolonged relapses (Murphy, 1983), although Baldwin & Jolley (1986) have recently reported a more favourable outcome. Various researchers have looked for predictors of a good and poor prognosis (Burvill *et al*, 1986). Some authors (e.g. Kay *et al*, 1955; Post, 1972; Cole, 1983) have drawn a distinction between early-onset depression, that is, the first ever episode of depressive illness occurring before the age of 60 years, and late-onset depression, the first episode occurring after the age of 60 years. Late-onset depressives have been said to have better pre-morbid personalities and less family history of depression than early-onset depressives (Kay, 1959; Hopkinson, 1964; Post, 1972). There is evidence that adverse life events occur with greater than chance frequency where there is depression in younger patients (Paykel *et al*, 1969; Brown *et al*, 1973), and that similar factors contribute to the onset of depression in old age (Murphy, 1982). Post (1978) pointed out that the kind of life events shortly preceding nearly 80% of depressions are the common experiences of all old people, but that since only a few develop depressions there must also be present in the depressives some personality or biological predisposition. After reviewing the literature Cole (1983) concluded that the effect of age of onset on prognosis was unclear.

A relevant question for research is: why do some people develop depression for the first time at the age of 60, 70 or 80 years? Are the same aetiological factors that operate in depression beginning earlier in life relevant to late-onset depression, or are other factors operative? Post (1972) and Jacoby (1981) have raised the question of whether depression in old age may be partly due to a biological ageing process. Although they did not specify what was meant by 'biological ageing process', the reasonable presumption is that this term refers to physiological, biochemical and other cellular changes, including neuronal death, in those areas of the brain thought to be closely associated with affective disorders. Post did not differentiate between early-onset and late-onset depression, although Jacoby was clearly referring to late-onset cases. It is now generally agreed that the relationship of organic brain disease to affective disorder in the elderly is an unresolved question (Jacoby *et al*, 1980). In a comparison of head computerised tomography (CT) scan results in normal, depressed and demented elderly, Jacoby *et al* (1980) suggested that the emergence of depression in old age is facilitated by the biological process of ageing, which is reflected in the central nervous system by ventricular enlargement. Eight out of the nine of their subgroup of in-patient elderly depressed patients who had ventricular enlargement, and subsequently a very poor two-year prognosis, were late-onset depressives.

Studies of elderly people in hospital (Kay & Roth, 1955; Roth & Kay, 1956) and in those living at home (Kay *et al*, 1964; Kay & Bergmann, 1966) have shown that physical illness is important not only in the aetiology of organic syndromes but also in the functional syndromes of old life. Poor prognosis of depression in the elderly has been associated with chronic physical health problems (Murphy, 1983; Roth, 1983; Baldwin & Jolley, 1986) and with cerebral organic illness (Post, 1972). The high incidence of depressive illness following strokes has been well documented by Robinson *et al* (1984), although some of these findings are still controversial (House, 1987).

These findings suggest that biological factors may be more important in late-onset than in early-onset depressives. There is the further possibility that in early-onset depressives biological processes associated with ageing are superimposed upon the clinical state present since an earlier age. Depressive episodes become more frequent with increasing age in those whose depression first developed at an earlier age (Post, 1972). Post (1978) has claimed, on the basis of his long clinical experience and research with elderly depressives, that the failure of elderly depressed patients to respond to adequate treatment, when they have been treated successfully in earlier life, is usually due to the development of a persistent physical disorder.

This study examines whether there were any differences between cases of an early-onset and late-onset depression in a cohort of depressed elderly patients under psychiatric care. On the basis of the relatively scanty evidence in the literature we hypothesised that, compared with early-onset depressives, late-onset patients would have less family history of depression and more stable pre-morbid personalities; major life events would be less important in the onset of the depression; a higher proportion of cases would have endogenous depression, and they would have more cognitive impairment; and both cerebral and non-cerebral physical illness would be more prevalent. There was no strong reason to expect any difference for severity of depression between early- and late-onset cases.

Method

This study formed part of a study of prognosis of depressive illness in the elderly. The cohort consisted of 103 patients who were being treated for a depressive illness by psychiatrists in a number of public psychiatric hospitals in Perth, Western Australia. For entry to the study patients must have been aged 60 years or over, have an adequate command of English to participate in the research process, and have a primary diagnosis of DSM–III major depressive illness (American Psychiatric Association, 1980) that had been present for at least four weeks. The cohort of 103 patients were consecutive patients meeting the criteria.

Each patient was seen by a psychiatrist (PWB or HGS) or a third-year psychiatric registrar (all trained to administer the research instruments), and the following were completed: Geriatric Mental Schedule – Shortened Version (Henderson *et al*, 1983), Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), Mini Mental Status Examination (MMSE; Folstein *et al*, 1975) and Newcastle Rating Scale (Carney *et al*, 1965). A clinical assessment of pre-morbid personality was performed. Family history of psychiatric illness was obtained only from the patient. Unfortunately, inquiry on this point and about pre-morbid personality was not made of relatives and key informants. An assessment was made of the severity of each patient's physical health, with acute and chronic illness differentiated (Burvill *et al*, 1989). In addition, an OARS Physical Health Rating (Duke University Centre, 1978) and a patient Self-Health Rating were completed. Each patient was assessed by the psychiatrist on whether he/she was an early-onset or late-onset depressive, depending upon whether the first-ever episode of depression began before or after the age of 60 years.

After the clinical assessment, each patient was seen by a psychologist graduate research assistant and the following were assessed: demographic information, Eysenck Personality Inventory (EPI), Major Life Events and Difficulties according to Brown's method (Brown & Harris, 1978) suitably modified for the elderly, and the availability of confidants. As part of the larger study, EPI scores were measured on a randomly selected community sample of 85 non-depressed 'normals', matched with the depressives for age and sex.

The cohort of 103 patients came predominantly from two general hospital psychiatric units in Perth's two largest teaching hospitals. A total of 69 patients came from one of those hospitals, comprising 55 in-patients, five out-patients, and nine subjects of consultations from the Geriatric Service (all in-patients). There were 16 in-patients and two day patients from the second hospital. A further seven in-patients came from a third general psychiatric unit in the latter part of the survey. The remaining nine patients came from mental hospital in-patients (seven) and a psychogeriatric in-patient facility (two).

Data analysis

Two types of analysis were performed to compare characteristics of elderly depressives with early-onset and late-onset illnesses. First, univariate comparisons were performed by means of χ^2 and t-tests for each of the individual demographic, life event, psychiatric and physical illness measures. Second, to take account of correlations between the individual measures (and hence the outcomes of the univariate comparisons), the early-onset and late-onset cases were simultaneously compared for introversion, neuroticism, family history, sex of subject, DSM–III severity, and scores on the HRSD, the Newcastle Endogenous Depression Scale, and the Mini Mental State Examination, by means of a discriminant function analysis. This analysis selected that linear combination of these measures which maximally discriminated between the early-onset and late-onset cases. The contribution that each variable makes to the discrimination is indicated by the coefficient that it receives in the linear discriminant function (Harris, 1985).

Results

Demographic

By chance there was an almost equal number of early-onset (52) and late-onset (50) depressed patients in the cohort, with an equal sex distribution (M : F 1:1.8) in each category. The majority of the early-onset patients (85%) were in the

TABLE I
Age distribution of the early-onset and late-onset depressives

	60–64	65–69	70–74	75–79	80–84	85–89	Total
Early onset	18	13	13	6	1	1	52
Late onset	5	5	11	12	11	6	50

TABLE II
Comparison of mean EPI scores between early-onset, late-onset depressives and community controls

	Depressed		*Community*
	Early onset	*Late onset*	*controls*
Neuroticism	14.02	12.24	6.64
Extraversion	8.87	10.24	11.28
Early-onset v. late-onset depressives	Neuroticism	$t=1.481$,	d.f. = 90, NS
	Extraversion	$t=1.420$,	d.f. = 90, NS
Early-onset v. community controls	Neuroticism	$t=8.413$,	d.f. = 122, $P<0.001$
	Extraversion	$t=2.842$,	d.f. = 122, $P<0.001$
Late-onset v. community controls	Neuroticism	$t=6.361$,	d.f. = 122, $P<0.001$
	Extraversion	$t=1.273$,	d.f. = 122, NS

60–74-year age group and the majority of the late-onset patients (58%) in the 75–89-year age group (Table I). About half the late-onset depressives had had one or more previous attacks of depression since the age of 60 years, and half were having the first-ever episode of depression.

Life events and personality

There was a higher proportion of late-onset depressives (44%) who had a severe life event in the 12 months before onset of depression than of early-onset depressives (31%). However, this difference was not statistically significant.

As assessed by the EPI, there were no significant differences between the early-onset and late-onset depressives for the degree of neuroticism (Table II), but both had significantly ($P<0.001$) higher neuroticism scores than did the community 'norms'. The early-onset, but not the late-onset, depressives had a significantly ($P<0.01$) lower extraversion score than did the community 'norms'. However, although the extraversion scores were lower for the early-onset than the late-onset depressives, the differences were not significant. A clinical assessment of pre-morbid personality was made by the psychiatrist on a wide spectrum of personality traits, similar to the method used by Mann *et al* (1981). Only three personality traits were found in sufficient numbers for analysis, namely, anxiety, obsessional and dependency traits. A greater proportion (76.9%) of early-onset depressives had pre-morbid anxiety traits compared with late-onset patients (47%) ($\chi^2=9.76$; d.f. = 1; $P<0.002$). There were no significant differences for obsessional and dependency traits.

Psychiatric

The early-onset depressives, as measured both by the DSM-III diagnosis and the HRSD, were more severely depressed. A higher proportion of early-onset depressives (45%) had a DSM-III diagnosis of major depression with psychosis and a lower proportion (22%) major depression without melancholia than the late-onset patients (24% and 41%, respectively) (Table III). The early-onset cases had a HRSD mean of 23.5 and the late-onset cases of 20.4 ($t=2.679$, $P<0.01$).

Of both early-onset and late-onset depressives, 82% had endogenous depression as measured by the Newcastle Scale. Nine (18.4%) early-onset and 13 (27.1%) late-onset depressives scored in the 'organic' (<24) range of the MMSE. Only one patient (late-onset) scored in the severe range (score = 18). These differences were not statistically significant, although the discriminant function analysis (Table III) showed the early-onset depressives to have a significantly higher mean MMSE score. Of the early onset, 56% and of the late-onset depressives, 39% had a family history of depressive illness, but these differences were not statistically significant. Only four early- and two late-onset depressives reported a possible, and two late-onset depressives a definite, family history of other psychiatric illnesses.

TABLE III
DSM-III diagnoses (percentages)

Diagnosis	*Early onset*	*Late onset*
Major depression	22	41
Major depression with melancholia	33	35
Major depression with psychosis	45	24
Total	100	100

Physical illness

The health status of each group was assessed on ten variables (three of acute illness, three of chronic illness, the OARS, and three of the patients' own health rating). Although there was more chronic illness among the late-onset depressives, a discriminant function analysis failed to detect any statistically significant difference between the early-onset and late-onset depressives for any of these variables. The physical illnesses were predominantly chronic illnesses, of which 92% were non-cerebral. The severity of the small number of cerebral illnesses did not differ between early-onset and late-onset cases.

A CT brain scan was performed on only 26 patients, 13 early-onset and 13 late-onset depressives. There was a higher proportion of organic features in the late-onset (five patients) than the early-onset (one patient) depressives. In addition, one patient from each group showed greater than normal cerebral atrophy (when data were adjusted for age). The one early-onset case (a patient aged 60 years) showed an anterior communicating aneurysm, an *in situ* shunt and an early hydrocephalus from a cerebral episode and neurosurgical operation 12 months earlier. Of the five late-onset patients with organic CT features, three (aged 80, 81 and 85 years) were secondary to strokes, the changes in one (aged 67 years) were consistent with a long history of heavy drinking and one (an 81-year-old) showed signs of congenital hypoplasia of the left cerebellar and inferior vermis.

Multivariate comparisons

Table IV shows the results of a discriminant function analysis comparing early-onset and late-onset depressives for a number of factors. Early-onset depressives were significantly more likely to have a higher MMSE score, and to be more severely depressed when measured both by the DSM-III classification and by the HRSD. The late-onset depressives were significantly more extraverted on the EPI Scale. There were no significant differences for the degree of neuroticism, for the family history of depression, and for the number of endogenous v. neurotic depressives on the Newcastle Scale.

TABLE IV

Discriminant function analysis of a number of factors attempting to discriminate between early-onset and late-onset depressives

Factor	*Canonical coefficients*
Introversion	0.378[1]
Neuroticism	0.043
Family history	0.164
Sex of patient	0.117
DSM-III severity	0.471[1]
HRSD	0.418[1]
Endogenous depression	0.163
MMSE	0.515[1]

1. Statistically significant coefficients.

Discussion

No statistically significant differences were found for the predisposition to become depressed as measured by family history, neuroticism, pre-morbid personality or life events, although the differences in family history were substantial and in the direction predicted. By contrast, the finding for life events was in the opposite direction to that predicted. Clinically, in the early-onset cases, patients were more severely depressed as measured by the HRSD and DSM-III. In both early-onset and late-onset cases, patients were endogenous rather than neurotic depressives, as measured by the Newcastle Scale. Efforts to show a postulated greater biological impairment among the late-onset cases produced mixed results.

Before discussing the significance of these findings we need to consider the possible biases in the selection of the sample, and any limitations these impose upon our conclusions. The initial selection of patients for the study did not take into account the factor of early-onset v. late-onset of depression. It was purely fortuitous that the two groups had an equal sex distribution and were of the same size. The sample represented those elderly depressed patients seen by busy general psychiatrists, in their everyday work in a hospital system, in which very few elderly depressed patients were treated by a small psychogeriatric service. The majority were in-patients. The psychiatric unit, in which over half the study cohort were seen, had close links with an active geriatric unit, and as such, saw a number of late-onset depressives aged 75 years and older, representing about 14% of the late-onset depressives. Rigorous inquiry revealed that very few elderly depressives were treated in private hospitals by psychiatrists during the time of the survey. Thus the cohort seemed a fairly representative sample of severe elderly depressives treated by Perth psychiatrists.

The late-onset group was definitely older than the early-onset group, although patients of both groups were represented in all five-year age groups from 60–64 to 85–89 years of age. It is clear that early-onset depressed patients can continue to become depressed until a later age, and conversely that some people can reach a fairly old age before first becoming depressed. There are several possible reasons for the decreasing frequency of early-onset depressives with increasing age. As early-onset depressives grow older, the frequency of attacks of depression may decrease. However, Post (1978) has expressed the opposite view, that as these patients grow older attacks of depression became more frequent, more protracted, and more difficult to treat. A more likely explanation is that as early-onset depressives grow older, a high percentage of them will have died, or have been placed in nursing homes or some other form of institution. Accordingly, a much smaller proportion of early-onset depressives will be living in the community. Nearly all the patients in this study lived in a non-institutional setting. By contrast, the older, late-onset depressives came from those who survived into old age, without developing depression at an earlier age, and who were still living in the community rather than in institutions. Thus, they come from a relatively robust group – the survivors of their generation. Hence it is reasonable to postulate that they needed something 'extra' to precipitate depression after having lived for most of their long life without the occurrence of any depressive illness. It is quite likely that the occurrence of these precipitants, especially if they are biological, increases with age.

It was hypothesised that there would be a greater predisposition to depression among the early-onset depressives as indicated by family history, pre-morbid personality, neuroticism and life events. The support for these predictions was weak. There was a difference in the predicted direction for the finding for family history (56% v. 39%) but the sample size was not large enough for this difference to be statistically significant. On the basis of this result it would be unwise to rule out a difference because the confidence intervals (CIs) around the proportion with a family history are consistent with there being a substantial difference in the proportion of elderly depressives (CI for early cases is 0.45–0.67 and 0.28–0.50 for the late-onset cases). A wide range of psychiatric illnesses, especially alcoholism, has been found to be present in excess in the families of depressed patients (Winokur *et al*, 1975) but, in this study, only a very small number of early-onset and late-onset cases gave such a family history.

For pre-morbid personality, there were difficulties in assessing the trait with confidence. We were not fully satisfied with the objectivity and stringency of our attempts to assess pre-morbid personality traits clinically, in spite of this being a long-standing clinical practice which is usually considered to be of major importance in the assessment of patients. Only one significant trait difference was detected, namely, that the early-onset depressives were more anxiety prone. Without accurate confirmatory history from informed relatives or friends, it was difficult to be sure that this trait was a true personality characteristic, or the gradual evolution over time of mild anxiety symptoms which were present for variable periods between the major attacks of depression – a phenomenon often seen clinically in such patients once the depressive illness has been successfully treated. Although a predominance of obsessional personality traits in depressive illness, especially those with more endogenous features, has long been noted by psychiatrists, the presence of this trait was not found to be a differentiating factor between early-onset and late-onset cases.

A related difficulty arises with trait neuroticism. Neuroticism was higher in the depressed than in the community sample, but this may have been because the depressed state coloured the way in which patients completed the EPI, irrespective of whether the depressive illness was of early or late onset. The patients could have been greatly influenced by feelings of negativism, anxiety, apprehension and uncertainty secondary to their depression, and consequently they may have answered the EPI questions as if they had been depressed for many years. The alternative of obtaining information from a reliable informant was not available to the researchers. Only reassessment of their personality, by the EPI when the patients are not depressed, would eliminate this possibility. The authors plan to conduct such an assessment as part of their 12-month follow-up study.

Should it be found that the EPI findings remain stable between the depressed and the non-depressed phases, the finding of a significantly increased neuroticism in both early-onset and late-onset depressives demands explanation. It is possible that excessive neuroticism is a risk factor for the development of depression in this age group, irrespective of whether or not the depression is clinically endogenous in type, or has a predominantly biological base, or is of early or late onset. Stressful life events are more likely to precipitate depression in those with excessive neuroticism. Likewise, minor cerebral organic changes may be more likely to lead to depressive illness in those with excessive neuroticism.

Much has been written of the role of severe life events in the aetiology of depressive illness in the younger age groups, especially by Brown & Harris (1978). In this study severe life events occurred more often in the depressive sample than in the community sample, confirming the earlier finding of Murphy (1982) for elderly depressives. However, there were no significant differences for the proportion of severe life events between early-onset and late-onset depressives. Actually there was a non-significantly greater number of life events in the late-onset cases, which is in the opposite direction to that hypothesised. These findings have been considered in detail by Emmerson *et al* (1989). The fact that more than half of each group did not have a prior severe life event indicates that such events, although important, are not essential for the development of depression in the elderly.

Both early-onset and late-onset depressive groups showed the full range of severity of depression, but the late-onset group as a whole were clearly less severely depressed, whether judged by HRSD score, or on DSM criteria. This suggests that Post (1978) is right in believing that patients with a long life history of recurrent depression suffer from more severe episodes as they grow older.

Less than one-fifth of patients in either the early-onset or late-onset cases were neurotic depressives, with no differences between the two groups. There are a number of possible interacting explanations of these findings. The differentiation between endogenous and neurotic depression may be of less importance in the elderly. It is possible that depressive illness shows more endogenous features with increasing age, irrespective of whether the depression is of early or late onset. Younger depressed patients are more likely to be neurotically depressed and older patients to be endogenous (Post, 1982; Klerman, 1983). As with most published studies of depressive illness in the elderly, the present study was composed predominantly of in-patients who are at the more severe end of the spectrum of depressive illness, thereby increasing the likelihood of their being diagnosed as suffering from endogenous depression. That is, the cohort is not necessarily representative of depressive illness in the elderly in the wider community, but only of that presenting to psychiatrists for treatment.

It was hypothesised that the late-onset depressives would have a greater degree of biological impairment, as assessed by cognitive impairment and the presence of both cerebral and non-cerebral physical illness. We had too few patients to be able to provide a strong test of this hypothesis. However, there was some evidence in its favour, namely, greater cognitive impairment in the late-onset depressives and CT scan results in the predicted direction.

The possible role of physical illness in the aetiology of depression probably differs for cerebral and non-cerebral illnesses. The mechanism of the relationship is not straightforward and is not well documented in the psychiatric literature. It would be expected that in most non-cerebral illnesses the relationship is more in the nature of a psychological reaction to having the illness rather than to any direct biological connection. However, the close connection of depressive illness with endocrine disorders and with certain malignancies is well known. In the present study two patients had a malignancy diagnosed after the initial diagnosis of definite major depression was established. With cerebral illness, biological factors would be expected to have the predominant role.

A major expectation of the study was that there would be a higher incidence of physical illness, both cerebral and non-cerebral, in the late-onset depressives, which was independent of the age of the patient. The results showed this not to be so. The small non-significant excess of chronic physical disability in the late-onset depressives was easily explainable by the greater age of these patients. Although a greater proportion of the late-onset depressives showed abnormalities on head CT scan, the small number of scans performed (one-quarter of each group) was too small to allow any definite conclusions to be drawn. It was disappointing that CT scans were not able to be done on all patients, as this may have definitely supported or refuted the biological hypothesis. Nevertheless, the findings were in the direction hypothesised. Three of the five late-onset depressives with abnormalities were suffering from depression following strokes. The higher incidence of depression after strokes has been well documented by Robinson *et al* (1984), as have possible neuroanatomical/neurochemical aetiological mechanisms (Lipsey *et al*, 1984). The fourth case showed changes consistent with the patient's history of alcoholism, which could well have been a major factor in the genesis of late-onset depression. The only patient with early-onset depression with a CT abnormality had changes secondary to neurosurgical intervention just before the age of 60 years.

Conclusion

Most of the hypotheses tested failed to be supported. However, for reasons of statistical power consequent upon the number of cases studied, it would be unwise to rule out some of the hypotheses, especially those relating to family history predisposition and biological impairment. In the latter two the differences were in the direction hypothesised, although they did not reach statistical significance. There was no difference between the early-onset and late-onset depressives for the degree of neuroticism and for the proportion with endogenous depression. For severe life events, the differences were in the opposite direction to that hypothesised, even though not statistically significantly so.

There is a great need for more sophisticated laboratory measures of cerebral biological factors to ascertain adequately whether there was a greater degree of biological impairment in the late-onset cases. Such measures would include head CT scans, NMR and PET studies – all of which can, we hope, from page 673 to 679

subtle changes than the clinical measures the present study.

must be emphasised that many of the this and other published studies of llness in the elderly are based on cases nts with severe depression present for treatment, and do not necessarily apply rically large and clinically wide range of llnesses in the community.

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Platelet Monoamine Oxidase Activity and 5-Hydroxytryptamine Uptake in Agoraphobic Patients

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Platelet MAO activity and platelet serotonin uptake were determined in 20 agoraphobic and 16 neurotic depressive out-patients, and 19 healthy volunteers. Agoraphobic patients were characterised by significantly higher mean values of platelet MAO activity compared with the other two groups, while neurotic depressive patients exhibited significantly higher maximum platelet serotonin uptake velocity. These findings are compatible with an abnormality in the uptake and metabolism of serotonin.

In recent years the evaluation of the activity of monoamine oxidase (MAO) in human platelets has rapidly gained importance in the study of psychiatric disorders. Thus, the activity of this enzyme has been reported to be reduced in schizophrenic and bipolar depressive patients and increased in unipolar depressive patients (Coper *et al*, 1979; Rotman, 1982). However, little work has been carried out to study possible alterations in the activity of the enzyme in patients suffering from anxiety states, and, in particular, from phobic disorders. Increased levels of platelet MAO activity have been reported in a group of patients with chronic anxiety (Mathew *et al*, 1981). In such patients both anxiety and platelet MAO activity decreased following the application of relaxation training (Kralik *et al*, 1983). Platelet MAO activity was also found to be higher in agoraphobic than in non-agoraphobic depressed patients and healthy controls (Yu *et al*, 1983). Such an increase in MAO activity has also been confirmed in patients with panic disorders (Gorman *et al*, 1985). Sheehan *et al* (1984) noted significant positive correlations between MAO activity and clinical ratings of fear and anxiety, although enzyme activity was not elevated in agoraphobic patients with panic attacks. Khan *et al* (1986) found no differences in enzyme activity among panic disorder, generalised anxiety, agoraphobic, depressed and healthy subjects. A decrease in platelet MAO activity was reported in panic disorder patients (Balon *et al*, 1987*b*).

Several animal studies support the conclusion that there is involvement of 5-hydroxytryptamine (5-HT) when conflict behaviour is present (Braestrup & Nielsen, 1982), and, therefore, an involvement of 5-HT when anxiety is present may be inferred (File, 1984). However, clinical experience has not yet substantiated such a hypothesis. Neither Charney & Heninger (1986) nor Balon *et al* (1987*a*) could find any abnormalities in 5-HT metabolism and function in patients with panic anxiety. A decreased uptake of this amine has been reported to occur in the platelets of depressed patients (Tuomisto & Tukiainen, 1976; Meltzer *et al*, 1981).

In the present paper we report our findings for a group of agoraphobic non-depressed patients in relation to a group of non-agoraphobic depressed patients and healthy control subjects. We measured platelet MAO activity and estimated platelet 5-hydroxytryptamine uptake in all our subjects, and attempted to relate these two biochemical parameters to each subject's psychiatric state.

Method

Subjects

The agoraphobic group comprised 20 out-patients (18 females and 2 males, mean age 30.8 ± 8.2), selected on the basis of the DSM-III criteria (American Psychiatric Association, 1980). The following additional selection criteria were used: duration of present illness equal to or greater than one year; absence of features indicative of and/or diagnosis of major affective disorder, schizophrenia, organic brain syndrome, obsessive–compulsive disorder and alcohol or other drug abuse.

The neurotic depressive group comprised 16 out-patients (11 females and 5 males, mean age 32.8 ± 9.2), selected on the basis of the DSM-III criteria. The following additional selection criteria were used: duration of present illness equal to or greater than two years; absence of features indicative of and/or diagnosis of agoraphobia, major affective disorder, schizophrenia, organic brain syndrome, obsessive–compulsive disorder and alcohol or drug abuse.

The control group comprised 19 healthy subjects (11 females and 8 males, mean age 27.5 ± 7.6), who were randomly selected. Subjects in this group had no previous history, or family history, of any psychiatric disorder, and none was a relative of any of the patients.

All our patients were free from all psychotropic medication, for at least two weeks before the first biochemical sampling, and as all our patients were treated by behavioural techniques, they remained drug free throughout the duration of the study.

A number of non-psychiatric variables have been reported to affect the stability of platelet MAO activity (Sandler *et al*, 1981). Consequently, each prospective subject underwent careful clinical examination and routine screening in haematology and clinical pathology, so as to exclude conditions known to alter MAO activity, such as megaloblastic anaemia (Glover *et al*, 1980), non-alcoholic liver disease (Fowler *et al*, 1981), iron deficiency anaemia (Woods *et al*, 1977), migraine headache (Sandler *et al*, 1974) and insulin-dependent diabetes (Zeller & Davis, 1980). In females, since platelet MAO activity varies during the menstrual cycle (Baron *et al*, 1980), blood sampling was carried out on the equivalent day of the menstrual cycle, for each female subject, in addition to the above-mentioned screening. Finally, because physical exercise can cause a temporary increase in platelet MAO activity (Gawel *et al*, 1977), special precautions were taken for all subjects before each experimental session (see Biochemical study below).

Psychiatric assessments

These were carried out by the following procedures.

Present State Examination (PSE; Wing et al, *1974)*

Each patient in the study was interviewed at the beginning of the study by the standardised diagnostic instrument. Only patients satisfying the ICD–CATEGO criteria for a case were included in the study.

Brief standard rating for phobic patients (Marks & Mathews, 1979)

This standardised 'Fear Questionnaire' was completed by every patient at the beginning of the study, before the first biochemical sampling and the start of the treatment. Subsequently, the questionnaire was completed by every agoraphobic patient at fortnightly intervals until the end of the study. The self-rating form yields the following four scores: main target phobia (reflecting avoidance of the main phobic situation), global phobia (reflecting both distress and avoidance), total phobia (including five items for agoraphobia), and anxiety–depression (containing the five commonest non-phobic symptoms found in phobic patients).

The diagnostic assessment and the psychological ratings were carried out *blind* of the biochemical investigation and vice versa.

Biochemical study

Before a blood sample was taken each patient or healthy volunteer was allowed to relax for 30 minutes and to adjust to the physical environment of the clinic. A 40 ml blood sample was obtained from each patient and control subject. For the MAO assay, 20 ml blood were collected into acid citrate dextrose (4°C), and for the assay of 5-HT uptake, 20 ml into 3.8% sodium citrate (4°C). The time between blood sampling and the initial centrifugation stage for the preparation of platelet-rich plasma (PRP) was never more than 30 minutes. For both studies PRP was obtained by centrifugation of the blood sample at 200 *g* for 10 minutes at room temperature.

Monoamine oxidase assay

Blood platelets were isolated from PRP by centrifugation at 1000 *g* for 10 minutes at room temperature, and the platelet pellet obtained was resuspended in isotonic saline, and frozen and stored at $-20°C$ until required for the assay, which was performed within 3 weeks of the sample being obtained. Each platelet preparation was thawed and re-frozen twice before assay. The MAO activity in each platelet sample was determined using the method of George & Jones (1976), based on the assay of Robinson *et al* (1968), with $[^{14}C]$-tyramine hydrochloride as substrate, obtained from Amersham UK. Prior to the assay, non-radioactive tyramine solution was added to the radioactive amine to obtain a working solution of 10^{-2} mol/l concentration and a specific activity of 0.3 μCi/μmol. The protein concentration of each platelet assay sample was determined by the method of Lowry *et al* (1951).

5-HT uptake assay

5-HT uptake was determined in preparations of PRP obtained from each patient or control blood sample, as described above. Before assay the PRP obtained was thoroughly mixed. Each assay was begun within 45 minutes of the blood sample being obtained from the subject. The kinetics of active 5-HT uptake into platelets were determined for a 10-second period by the method of Gordon & Olverman (1978), as modified by Flaskos & George (1981), and with 5-hydroxy side chain-2$[^{14}C]$ tryptamine creatinine sulphate (58 mCi/mmol), obtained from Amersham UK. Uptake was measured in triplicate assays at four different final 5-HT concentrations in the range 10^{-7}–10^{-6} mol/l, and expressed as pmol/(mg protein 10 s). The separation of the platelets from the plasma after termination of uptake was attained by centrifugation at 8730 *g* for 1 minute at room temperature. The protein concentration in each assay sample was determined as for MAO. The V_{max} (maximum uptake velocity) and k_m (affinity constant) for 5-HT uptake in each platelet sample were determined from reciprocal plots of 5-HT incubation concentration v. uptake velocity (Lineweaver–Burke plot).

Statistical analysis

In this study diagnostic groups were not precisely matched for age, sex and time of blood sampling (Tables I and II). Observed differences between groups with respect to either MAO activity or 5-HT uptake could, therefore, merely reflect differences in these factors. Thus, an analysis of covariance was employed to examine the influence of each of these variables on MAO and 5-HT uptake respectively. The analysis consisted of an examination, within the group of patients, of two-way interactions of the group, according to sex, age and time of blood sampling.

To evaluate any relationship between symptom scores and either of the two biochemical variables, two separate cross-sectional analyses were employed. The first analysis involved the correlation of the average scores for each question of the Fear Questionnaire with the mean values of:

TABLE I
Diagnostic and epidemiological variables, mean platelet MAO activity and clinical diagnosis

Diagnostic group	*Age*[1] *(years)*	*Sex*	*Time of blood sampling*	*MAO activity (nmol/mg protein 30 min)*	*Effect of diagnosis and sex on MAO activity (nmol/mg protein 30 min)*	
					Females	*Males*
Agoraphobic ($n=20$)	30.8 (±8.2)	18F, 2M	12 a.m., 8 p.m.	15.650** (±8.158)	15.982 (±8.557)	12.662 (±0.202)
Neurotic depressive ($n=15$)	30.9 (±8.7)	10F, 5M	10 a.m., 5 p.m.	7.286 (±3.897)	7.717 (±3.853)	6.424 (±4.285)
Healthy control ($n=19$)	27.5 (±7.6)	11F, 8M	12 a.m., 7 p.m.	8.693 (±4.725)	10.508* (±5.314)	6.197 (±2.181)

1. Means ± s.d.
*$P<0.05$ compared with males of the same diagnostic group.
**$P<0.01$, agoraphobic compared with healthy control.

TABLE II
Diagnostic and epidemiological variables, 5-HT uptake kinetics in the diagnostic groups and clinical diagnosis

Diagnostic group	*Age (years)*	*Sex*	*Time of blood sampling*	k_m* *(μmol/l)*	V_{max}[1] *(pmol/mg protein 10 s)*
Agoraphobic ($n=19$)	31.1±8.2	17F, 2M	11 a.m., 8 p.m.	0.499±0.289	18.105±10.517
Neurotic depressive ($n=19$)	32.8±9.2	11F, 5M	12 a.m., 4 p.m.	0.526±0.273	26.228± 6.507*
Healthy control ($n=19$)	27.5±7.6	11F, 8M	12 a.m., 7 p.m.	0.432±0.231	18.851± 8.265

1. Means ± s.d.
*$P<0.01$.

(a) platelet MAO activity
(b) 5-HT uptake V_{max} and
(c) 5-HT uptake k_m.

The second analysis involved the correlation of the scores for each section of the PSE schedule with each of the previously mentioned biochemical variables (a), (b) and (c). Patients' data were excluded from these statistical analyses if any of the biochemical values were missing or incomplete.

Results

Diagnostic and epidemiological correlations with platelet MAO activity and 5-HT uptake

Platelet MAO activity and 5-HT uptake were initially examined in relation to clinical diagnosis, without taking into consideration the possible effects of other variables, such as age, sex and time of blood sampling. The mean values of platelet MAO activity and of the kinetic parameters k_m and V_{max} of 5-HT uptake for each diagnostic group are shown in Tables I and II. It is apparent that, with regard to MAO activity, the agoraphobic group was characterised by a significantly higher mean enzyme activity than the other two groups of subjects, whereas, for 5-HT uptake, the neurotic depressive group was characterised by a mean V_{max} which was significantly higher than that in the healthy control group.

The mean platelet MAO activity was subsequently calculated separately for each sex within every diagnostic group, and the results of the analyses are shown in Table I. Although in every case women exhibited higher enzyme activity than men, this difference was statistically significant only in the healthy control group. A similar calculation of the kinetic parameters of platelet 5-HT uptake failed to show any differences in relation to sex.

Since variables such as age and time of blood sampling, besides diagnosis and sex, can conceivably affect platelet MAO activity and 5-HT uptake, and given the lack of perfect matching between the groups of our subjects with regard to these factors, we submitted our data to analysis of covariance (see Method above). Considering the *F*-ratios, only the diagnostic group significantly affected the activity of platelet MAO ($F=9.48$, $P<0.01$, d.f. = 2). Individual comparisons between diagnostic groups revealed that the significant effect was due to higher levels in the agoraphobic group. No significant interactions were revealed between the above variables with respect to MAO activity. With regard to 5-HT uptake, a similar analysis indicated that only one factor – diagnostic group – significantly affected the rate of uptake, neurotic depressives having higher levels of uptake than the other two groups ($F=3.32$, $P<0.05$, d.f. = 2). No significant interactions were revealed between the above variables in relation to either of the kinetic parameters of 5-HT uptake.

Platelet MAO activity, 5-HT uptake and phobic symptom rating

The scores of each section of the PSE schedule obtained from 33 patients (19 agoraphobic and 14 neurotic depressive) were correlated with the mean values of:

(a) platelet MAO activity and
(b) the kinetic parameters k_m and V_{max} of 5-HT uptake.

Of the PSE sections rated in this study, 'situational anxiety' exhibited a statistically significant positive correlation with MAO activity (correlation coefficient, $r=0.45$, $P<0.05$) and with the maximum velocity (V_{max}) of the active amine uptake ($r=0.51$, $P<0.01$). Statistically significant positive correlations were also shown between irritability and the substrate affinity (k_m) of the 5-HT uptake ($r=0.40$, $P<0.05$), and between 'reduction of interests' and k_m ($r=0.43$, $P<0.05$).

In a similar analysis, the scores from the Fear Questionnaire obtained from 32 patients (18 agoraphobic and 14 neurotic depressive) were correlated with the mean values of platelet MAO activity and the kinetic parameters k_m and V_{max} of 5-HT uptake. Platelet MAO activity was significantly positively correlated with the agoraphobic avoidance scores ($r=0.52$, $P<0.01$) and with the tense-panicky scores ($r=0.43$, $P<0.05$). This last symptom exhibited a statistically significant negative correlation with the kinetic parameter V_{max} ($r=-0.44$, $P<0.05$).

Discussion

Among the various manifestations of the agoraphobic syndrome, the degree of avoidance behaviour, as rated in this study (see Method), showed a much stronger positive correlation with the level of platelet MAO activity than did manifestations less characteristic of the agoraphobic syndrome, such as depression and irritability. Similarly, high positive correlations were found between the level of platelet MAO activity and the scores of 'tension' and 'panicky feelings' and the 'situational anxiety' ratings obtained in the agoraphobic subjects.

In our study, females exhibited a higher level of platelet MAO activity, although only in the case of the healthy group was this sex difference significant. This is in agreement with other investigators (Robinson *et al*, 1971; Murphy *et al*, 1976; Puzynski *et al*, 1983). Since 90% of our agoraphobic subjects were females, in accord with the known epidemiological data (Agras *et al*, 1972), it is important to establish that the higher level of MAO activity shown by our agoraphobic group was not the result of the preponderance of female subjects in it. As the analysis of covariance indicated, the separate effect on platelet MAO activity of classifying according to clinical diagnosis was significant, while the separate effect on the enzyme activity of classifying according to sex failed to attain statistical significance.

The possibility that some uncontrolled variables such as the stress of anxiety associated with venipuncture may play a role in the observed changes in platelet MAO activity cannot be excluded, as a two- to three-fold increase in the activity of this enzyme after venipuncture has been noted (Gentil *et al*, 1976). In our study each subject was allowed to relax for 30 minutes before a blood sample was taken. Certain personality characteristics have also been found to affect platelet MAO activity (Murphy *et al*, 1977; Schooler *et al*, 1978), and monotony avoidance and impulsiveness have been associated with low enzyme activity (Perris *et al*, 1984). However, in our study, no correlation was found between platelet MAO activity and the extroversion and neuroticism scores (Eysenck & Eysenck, 1964, unpublished).

MAO exists in two forms, A and B, with differing substrate affinities (Sandler *et al*, 1981). Platelet MAO is mainly type B, which shows the highest activity for benzylamine as substrate (Coper *et al*, 1979). This study was carried out using tyramine, which is a substrate for both types A and B. In two studies of platelet MAO activity where benzylamine and tyramine were compared the results obtained were similar (Mann, 1979; Coper *et al*, 1979).

In the present study we could not detect significant alterations in the activity of the platelet MAO among our neurotic depressive patients, and this result is in good agreement with the findings of Coper *et al* (1979), Davidson *et al* (1980), Gudeman *et al* (1982) and Yu *et al* (1983). The increased activity of this enzyme in non-endogenous depression reported by some investigators (Mann, 1979; White *et al*, 1980) could be accounted for by the effects of a preponderance of male or female subjects or by differences in diagnostic criteria and selection of patients.

In our study we could find no association between the 5-HT uptake kinetics and the central symptoms of agoraphobia. To our knowledge, no such association has yet been reported in the literature. This is in agreement with Charney *et al* (1986), who showed that 5-HT receptor sensitivity (in terms of the prolactin response to a tryptophan challenge) was unchanged in patients with panic anxiety disorders. Innis *et al* (1987) have shown that platelet ^{3}H-imipramine binding is unchanged in patients with panic anxiety. This is a further indication that the platelet 5-HT uptake site to which ^{3}H-imipramine may bind is unaltered in patients with panic anxiety. However, we found an increased platelet 5-HT uptake in our neurotic depressive group of patients (see Results). In contrast, in a study similar to ours, Hallstrom *et al* (1976) failed to show any increase in the 5-HT uptake among their neurotic depressed patients. However, these investigators' findings cannot be accepted without some reservations concerning the use of relatively high concentrations of radio-labelled serotonin, and long incubation periods, leading to determinations of platelet 5-HT uptake that were not made under conditions of initial velocity as in our study (see Method). Furthermore, in such conditions the contribution of non-saturable passive diffusion to the measured uptake of 5-HT increases considerably.

Codd & Walker (1987) have demonstrated that delay between blood sampling and assay, and also the type of anticoagulant used, may affect platelet 5-HT uptake. Thus, 5-HT uptake (using 2-minute incubation times) was significantly lower in platelets assayed more than 1 hour after venipuncture, whereas our assays were carried out within 45 minutes of sampling (see Method). They also demonstrated that platelet 5-HT uptake activity is better preserved in a citrate rather than an EDTA anticoagulant.

From a more theoretical standpoint, another group of investigators have found, independently, a significantly higher MAO activity in the platelets of a well-defined and clinically rated group of agoraphobic patients (Yu *et al*, 1983). Similarly, high levels in the activity of platelet MAO were reported previously (Mathew *et al*, 1981; Davidson *et al*, 1980) in the context of chronic, generalised anxiety. Moreover, a reduction in this activity was shown to occur in anxious patients following biofeedback relaxation (Mathew *et al*, 1981; Kralik *et al*, 1983). The nature of the relationship between platelet MAO activity on the one hand and anxiety and fear scores on the other is far from clear at present. Interesting in this respect is the report by Kralik *et al* (1983) of a decrease in the affinity of the substrate phenylethylamine for MAO in chronically anxious patients following relaxation training, but the exact process whereby chronic anxiety brings about this change in the substrate affinity is not known. An elevated activity of MAO has been demonstrated in animals subjected to prolonged or chronic stress (Alexander *et al*, 1980; Maura *et al*, 1978), and it has been suggested that in rats under stress, an increased release of ACTH leads to an elevation of adrenal MAO activity (Bhagat *et al*, 1973).

Seen in this context, the elevation in MAO activity reported here may represent a compensatory adaptation to increased noradrenergic and adrenergic activity under stress. As we have already indicated (Flaskos *et al*, 1984), it is difficult at this time to interpret whether such findings represent state- or trait-dependent variables, and more studies are required to enable us to answer this question.

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The Classification of Psychiatric Morbidity in Attenders at a Dermatology Clinic

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Of a random sample of new attenders at a dermatology out-patient clinic, 40% were classified as suffering from a psychiatric disorder. There was no correlation between psychiatric morbidity and the severity or site of skin disease. Self-report measures of the behavioural impact of skin disease and attitudes to appearance were related to psychological morbidity. Except in subjects without visible skin pathology (5%) there was no evidence that psychiatric illness was an aetiological factor in the development of skin disease. Self-report measures were used to distinguish between those patients in whom psychiatric morbidity was closely related to skin disease (75%), and those in whom it may be coincidental (20%). Psychological care for the former group is most appropriately provided by physicians, who should be encouraged to improve their detection and management of psychiatric morbidity.

Since the work of Shepherd *et al* (1966) there has been increasing awareness of psychiatric disorder in general medical and general practice settings. Subsequent work (e.g. Goldberg & Huxley, 1980; Mayou & Hawton, 1986) has shown this to be common, disabling, often undetected, and to influence outcome (Querido, 1959; Hawton, 1981). Furthermore, accurate identification reduces psychological distress (Johnstone & Goldberg, 1976), and may influence both compliance and satisfaction with treatment. However, although there is evidence of a relationship between physical and psychiatric disorder, its nature has remained elusive because of problems of symptom overlap and case identification.

This study describes a preliminary attempt to classify psychiatric morbidity in a medical setting according to possible causes of the disorder. A dermatology out-patient clinic was chosen for two reasons. First, the symptoms of most skin diseases do not overlap with the somatic disturbances associated with psychiatric illnesses. Second, since skin disease is visible it is easy for the trained observer to distinguish between those with physical pathology and those without.

Most previous psychiatric studies of dermatology patients have been anecdotal (see Koblenzer, 1983; Musaph, 1976, for reviews). Older literature, and some not so old, has contended that many skin diseases have a significant psychosomatic aetiology (e.g. Alexander & French, 1948; Figueria & Faria, 1987; Resch *et al*, 1987; Van der Schaar & Couperus, 1986), and has emphasised the psychodynamic or symbolic significance of skin disease. This approach assumes that psychiatric morbidity is a cause of many common dermatoses. However, this model may be accurate only in those presenting to a dermatologist with psychiatric disorders mimicking skin disease (Sheppard *et al*, 1986). A variety of labels have been ascribed to such patients, including delusional hypochondriasis, dermatitis artefacta, dysmorphophobia and dermatological non-disease (Wessely, 1989). Little is known about their characteristics or prevalence, although there is preliminary evidence suggesting that high levels of psychopathology occur in many of these patients (Hardy & Cotterill, 1982; Owens & Millard, 1987; Wessely, 1989).

The alternative view, that skin diseases are a cause of psychiatric morbidity, has received little attention. The dermatological literature contains the occasional account of the social and emotional problems associated with certain skin diseases, such as psoriasis (Jobling, 1976) or acne (Kenyon, 1966). Although Kenyon (1962) screened 100 out-patients with a personality inventory, the first systematic study of psychiatric disorder in a skin clinic was by Hughes *et al* (1983). Both more extensive lesions and those on exposed parts of the body were associated with increased psychiatric morbidity, in keeping with a brief abstract (Shuster *et al*, 1975) relating the severity and site of acne with a decline in self-image and self-esteem.

Personal factors affecting vulnerability to the effects of skin disease have not been studied. For example, a cognitive theory of minor psychiatric disorder (e.g. Beck, 1976) would predict that those who develop mental disorder as a result of skin disease would be more likely to have perfectionist attitudes to their appearance. Similarly, no study has systematically assessed the effect of skin disease on a person's life. It is postulated that the greater the personal changes resulting from skin disease, regardless of objective severity, the greater the psychiatric morbidity.

The current study aims to classify psychiatric morbidity in the dermatology clinic, using standardised measures of psychiatric morbidity, skin pathology and the effect of skin disease. The specific hypothesis to be tested is that three groups of patients can be identified: those with skin disease resulting from psychiatric disorder, those with psychiatric disorder resulting from skin disease, and those in whom skin disease and psychiatric disorder are coincidental. It also examines the hypothesis that both personal attitudes to appearance and the effect of skin disease on a subject's life are related to psychiatric illness. Finally, it determines how good dermatologists are at detecting psychological distress.

Method

The sample was taken from new attenders at the Dermatology Out-patient Clinic of King's College Hospital, London. On each day selected, a random sample of all new patients aged over 18 were invited to take part in the study. The following assessments were performed.

(a) General Health Questionnaire (GHQ, 12-item; Goldberg, 1972). Those scoring 2 or more were defined as cases.

(b) Clinical Interview Schedule (CIS; Goldberg *et al*, 1970). The total weighted score was calculated and those who scored 13 or above were defined as cases.

(c) Attitudes to appearance (ATT). This was a new five-point scale, using semantic differentials to measure attitudes to appearance, modelled on the dysfunctional attitudes scales of Beck (1976). Patients were asked to agree or disagree on a five-point scale for each of the following questions:
   (i) If my appearance is not perfect, I feel self-conscious in public
   (ii) Physical appearance is only one small part of why people are attractive
   (iii) I feel inferior if my physical appearance is not perfect
   (iv) Other people will still like me, however I look
   (v) I can only go out in public if I look my best.

The items making up the scale were administered by an interactive computer program. Agreement with items 1, 3 and 5 and disagreement with items 2 and 4 were given positive scores. An overall score was calculated by adding the scores for each section. Those with more perfectionist attitudes scored more.

(d) Impact of skin disease (IMPACT). These questions, also administered by computer, asked about the effect of skin disease on the following areas of the subject's life: care over appearance, use of cosmetics, use of mirrors, self-avoidance of people, avoidance by other people, embarrassment about appearance, awareness of smell and development of sexual problems. Subjects were asked to rate changes occurring since the start of their skin problem. The scale was scored so that any change in behaviour since the development of the disease, whether an increase or a decrease, was given a positive value.

(e) Dermatology assessment. A standardised form was completed by the dermatologist, who recorded skin diagnosis, indicated the extent and location of visible disease and rated the patient on a five-point scale of emotional distress, identical to the scale completed at the conclusion of the CIS, the overall severity rating (OSR).

The participants were also asked to complete the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) and a computerised assessment for psychiatric disorder (Lewis *et al*, 1988). The results of these will be presented elsewhere.

Results

Characteristics of the sample

The sample consisted of 173 subjects. The average age was 42 years (range 18–85; s.d. = 18 years) and 58% were women. Of 13 patients who did not complete any assessment, one refused, and the others left before they could be contacted. Information was therefore collected on 92% of the sample.

The rest of the sample can be thought of as comprising three groups. Because of the limited availability of computers, only the first group of 89 completed all the assessments. The second group of 22 subjects completed only a GHQ while the third, 49 subjects, completed the CIS but not the computerised assessments. The third group included 14 subjects who were illiterate or partially sighted and who therefore could not complete the GHQ. Of the total sample, 80% were interviewed using the CIS.

The only statistically significant difference between the four groups was in terms of age, since those in the third, CIS-only, group, were older patients because partial sight was more common in the elderly. This group also showed a slightly longer duration of skin disease before presentation, probably also because of age. There was no difference between any of the groups in GHQ or CIS scores, in measures of dermatological morbidity or in the male/female distribution. Although complete data, including the assessments of ATT and IMPACT, were obtained on a smaller proportion of subjects, this was a representative group in terms of psychiatric morbidity.

Prevalence of psychiatric morbidity

We found an overall prevalence of psychiatric morbidity of 40.2% (51/133; 95% confidence interval (CI) 31.7–48.7%) by the CIS. Defining cases by questionnaire (GHQ) led to a prevalence of 42.7% (95% CI 38.6–46.8%). These figures are similar to those obtained for other medical out-patients (Goldberg, 1986; Mayou & Hawton, 1986).

At the end of the CIS the psychiatrist who administered the interview made an overall rating (OSR), and on this basis 14 subjects (9% of the total, 95% CI 4.2%–13.9%) were thought to require psychiatric treatment as outpatients, and only two required 'substantial' psychiatric care. The women had non-significantly higher scores on the CIS (male mean = 12.1; female mean = 13.4, $t = 0.67$; d.f. = 87, $P < 0.1$) and a slightly higher proportion (43% v. 36%) were classified as cases.

The majority were cases of minor affective disorder. Of the two cases of severe disorder, one patient received the diagnosis of delusional parasitosis and the second was a transvestite with a depressive illness and alcohol dependence.

Diagnostic category of skin disease and psychiatric disorder

The diagnoses made by the dermatologist were grouped into 11 categories (warts, seborrhoeic warts, naevi, psoriasis, eczema, acne, other single lesions, other widespread skin diseases, other diagnoses, alopecia, no visible lesion). A one-way analysis of variance indicated that there was no significant difference between the CIS scores ($F = 1.74$, $P < 0.1$) in the various categories.

There were eight subjects (5%; 95% CI 1.6%–8.4%) with no visible dermatological condition, and these were classified as having 'dermatological non-disease'. Of these, 62% (95% CI 45%–79%) were classified as cases by the CIS.

Attitudes to appearance

There was a symmetrical distribution of responses in the sample, with a mean of 1.4 (s.d. = 0.89). Cronbach's alpha, a measure of internal consistency (Cronbach, 1951), was 0.80. The midpoint of the five-point scale, indicating neither agreement nor disagreement, was 2.5. Only 10% of the sample scored more than 2.5, indicating overall agreement with the perfectionist attitudes; the majority were in disagreement. The women had slightly more perfectionist attitudes (male mean = 1.1, s.d. = 0.742, $n = 38$; female mean = 1.5, s.d. = 0.955, $n = 51$; $t = 1.89$; d.f. = 87; $P < 0.05$).

TABLE I
Correlations between important variables

	CIS	*ATT*	*IMPACT*
Attitudes to appearance	0.42** (0.27**)		
Impact	0.63** (−0.27**)	−0.46** (−0.28**)	
Proportion of disease on exposed areas	0.04 (−0.01)	−0.11 (−0.07)	0.29** (0.19*)
Area of skin involved: %	−0.01 (0.05)	0.00 (−0.02)	0.01 (0.10)
Duration of skin condition	0.03 (0.04)	−0.09 (−0.09)	0.23* (0.15)

*$P < 0.05$, **$P < 0.01$.
Kendall's tau is given in parenthesis.

This measure (ATT) was correlated with the CIS (Table I), independently of all other variables. This was more pronounced in the high-impact group (see below), suggesting that the attitudes measure was not just a reflection of psychiatric disorder. Furthermore, attitudes to appearance were unrelated to any characteristics of skin disease.

Impact of skin disease

There was a wide range of responses (from 0 to 15), with a marked skew to the right. Just over half (44/84) scored less than 2, indicating that the skin disease had virtually no impact. An arbitrary cut-off of less than 2 was therefore used to define those with low impact. This score (IMPACT) was correlated with CIS and with ATT (Table I).

Of the low-impact group, 20% were classified as cases, compared with 59.5% of the group with high impact (Table II). The high-impact group had higher CIS scores ($t_{87} = 62.1$, $P < 0.0001$) and lower ATT scores ($t_{87} = 16.8$, $P < 0.0001$). The correlation between ATT and CIS was greater in the group scoring higher for IMPACT (difference between the slopes $t_{84} = 5.45$, $P < 0.002$; Table II). The variance of ATT was slightly larger in the high-impact group (range 8–25; s.d. = 4.8) than in the lower group (range 8–25; s.d. = 3.9). The difference between the slopes is unlikely to result from this modest change in variance.

Women had higher scores than men for IMPACT (male mean = 2.2, s.d. = 3.01; female mean = 3.9, s.d. = 4.21; $t_{87} = 9.6$, $P < 0.01$).

Effect of duration, location and area of skin disease

There was no correlation between the total area of skin involved and CIS, ATT or IMPACT (Table I). The proportion of skin disease on exposed areas (face, hands, scalp and arms) was then calculated, and the sample was

TABLE II
The impact of skin disease

	Low impact	*High impact*
Proportion of cases of psychiatric disorder	20% (7.6 to 32.4%)	60% (44.6 to 74.3%)
Correlation between ATT and CIS	0.15	0.40
Slope of regression line, CIS v. ATT	0.34 (−0.23 to 0.90)	1.13 (0.51 to 1.74)
Detection by dermatologists		
Correlation between dermatologist rating and CIS	0.0	0.32
Slope of regression line, dermatologist rating v. CIS	−0.02 (−2.94 to 2.90%)	4.50 (0.30 to 8.76%)

95% CI in parenthesis.

divided into three groups: unexposed only (41%), mixed (20%) and exposed areas only (39%). Skin disease on exposed areas was associated with higher IMPACT scores, but not with CIS or ATT (Table I).

When subjects with single lesions were compared with subjects with all other diagnoses and those without visible lesions, there was no effect on CIS ($F = 1.83$, $P < 0.17$) but there was an effect on IMPACT ($F = 6.93$, $P < 0.002$), those with single lesions reporting lower impact.

Data on duration of skin disease before presentation to the clinic were sorted into five equal-sized groups. They were weakly related to IMPACT but not to CIS or ATT (Table I).

These results show a pattern, since none of the indices used to indicate extent, duration and location of skin disease was related to the measures of mental illness (similar results were generated if the dependent variable was the GHQ score), nor were any related to attitudes to appearance. However, the proportion affected or exposed and the duration of skin disease were related to the reported impact of the skin condition. These results were confirmed by Kendall's tau, a rank correlation method (Table I).

Further analysis

In order to explain the contribution of the different variables to psychiatric morbidity a multiple regression analysis was performed. With CIS as the dependent variable, a linear model including attitudes and impact was not significantly different from a model including all the variables of both psychopathology and skin disease. The regression coefficients of the complete model indicated that there were significant independent contributions of IMPACT ($t = 5.05$, $P < 0.0001$) and ATT ($t = 2.79$, $P < 0.01$), but there was no significant effect of sex of subject ($t = 1.79$, $P < 0.1$). No interaction terms were significant. The trend for higher rates of psychiatric distress in women may be explained by the male/female differences in ATT.

These results confirm that the effects of impact and attitude were independent of each other. None of the factors relating directly to skin disease, including diagnosis, was associated with psychological distress. The effect of duration of illness and area exposed was therefore explained by the impact score.

The relationship between skin disease and psychiatric disorder

The impact scale is a composite measure reflecting both the psychiatric disorder and the behavioural change resulting from the skin disease. It does not reflect any psychological construct, unlike the attitudes assessment, but was designed simply to record behavioural change. It is also a self-report measure of change occurring after the onset of skin disease. For that reason it may also serve to discriminate those in whom psychiatric disorder was related to skin disease, from those in whom it was coincidental. Those subjects who recorded low impact may thus be thought of as a group where any psychiatric morbidity was coincidental with the existence of skin disease. Validity is indicated by the different pattern of psychiatric morbidity, CIS and ATT correlations found between high- and low-impact groups (Table II). However, one cannot exclude the possibility that patients wrongly attribute a change in the use of cosmetics, willingness to go outside, etc., to their skin disease rather than to other potential causes of psychiatric disorder.

The impact scale has therefore been used as part of a classification of the observed psychiatric disorder:

(a) Dermatological disease that has resulted in psychiatric distress. These patients report that their life has changed since the onset of skin disease, perhaps because of disfigurement, social embarrassment etc., but was also influenced by pre-existing attitudes. They are classified as psychiatric cases, but may also be in the high-impact group. In this study the association between psychiatric 'caseness' and high impact was found in 30% of the sample, and in 70% of the psychiatric cases.

(b) Dermatological disease with coincidental psychiatric illness. These patients present with standard dermatological disorders, and are classified as psychiatric cases, but show low-impact scores, and may not show an unusual constellation of attitudes. This is reflected in the smaller slope of the regression line between ATT and IMPACT. This group constituted 10% of the sample, and 25% of the psychiatric cases.

(c) Psychiatric illness causing or mimicking skin disease. The skin complaint, either real or imaginary, is the consequence of a psychiatric disorder. Such disorders constituted only 5% of the sample, of whom just over half had psychiatric symptoms. However, the CIS measures manifest psychiatric distress. It does not record either unusual psychiatric symptoms, or a pathological absence of symptoms (Lloyd, 1983), both of which occur in this category.

Detection of psychiatric disorder by dermatologists

The correlation between the CIS and the dermatologists' ratings was 0.36, but between the CIS and the psychiatrists' rating (OSR) it was 0.89. The sensitivity of the dermatologists compared with the OSR was 65%, the specificity was 49% and kappa was 0.24 (95% CI: 0.06–0.42). The dermatologists tended to underestimate prevalence; the test bias was 0.82. If the criterion was those cases requiring psychiatric intervention (OSR$\geqslant$3), the dermatologists' sensitivity remained poor (5/13: 38.5%), although both cases of severe disorder (OSR = 4) were also rated maximally.

The dermatologists appeared to be better at detecting psychiatric disorder in the patients who scored high on the impact scale. The regression slope in the high-impact group was steeper (Table II) than in the low-impact group, although this was not quite significant at the 5% level ($t_{78} = 1.74$, $0.1 > P < 0.05$). Numbers were too small to permit calculation of sensitivity and sensitivity according to impact group.

Discussion

The results did not confirm the finding of Hughes *et al* (1983) that widespread lesions and disease affecting exposed parts, where one might suppose any psychological effect to be maximal, were associated with increased psychiatric morbidity. However, the results indicated that both these measures, in addition to duration of skin disease, were related to the impact score. The impact that results from skin disease appears to be both an intervening variable between skin pathology and emotional distress, and perhaps also the result of that distress.

The impact scale is, in part, a more sensitive indicator of psychiatric distress resulting from skin disease. Support for our finding comes from a preliminary account of the effects of acne and hirsutism on pre-menopausal women. Of those affected, 70% avoided social occasions as a direct result of their hirsutism, and these were the most likely to show significant levels of psychiatric distress (Barth *et al*, 1987).

Attitudes to appearance and psychiatric disorder

Unfortunately, the design of the study cannot exclude the possibility that the perfectionist attitudes detected result from the skin disease, and that they were not pre-morbid. However, if this was the case, one would expect some correlation between abnormal attitudes and measures of the length, site and severity of skin disease. None was found. Instead, it is striking that attitudes to appearance appeared more closely related to psychiatric disorder than did aspects of skin disease. This is consistent with cognitive theories that argue that the interpretation of an event and its meaning to the individual are important determinants of psychiatric disorder (Beck, 1976). A dermatologist has written that the "magnitude of the effect (disfigurement) will be related to the subject's self-image and how he relates to others. Any blemish, no matter how small, may be the focus of severe emotional problems in a given patient" (Eller, 1974).

The role of skin diagnosis

We found no difference in the pattern of psychiatric morbidity for the various common dermatoses. This does not lend support to arguments for a psychosomatic aetiology of any specific dermatoses, and instead suggests that any interaction with psychological factors is of a general nature.

Kenyon (1962) found that those with viral warts "stand out as being highly neurotic and extraverted"; in modern parlance, the "worried well". We did not find a higher level of distress in those with viral warts or naevi, in spite of the fact that many had presented after a publicity campaign concerning the risks of malignant melanoma; indeed, those with solitary lesions reported less impact on their lives rather than more.

In contrast, five of the eight patients without visible dermatological pathology were suffering from psychiatric illness. Although the prevalence of such disorders is low, comprising only 4.4% of this sample, they are not as rare as is suggested by reports based on cases referred by dermatologists to psychiatrists (Wessely, 1989), and are a significant cause of morbidity. It has been suggested that some of these conditions are 'depressive equivalents', such as glossodynia (burning tongue) (Koblenzer, 1983; Coles, 1966). However, we have shown that the majority of depressive illness encountered in the dermatological clinic presents in the conventional way.

Detection of emotional disorders by physicians

The detection of emotional disorders by physicians, as judged by entries in case notes, is generally poor (Mayou & Hawton, 1986). Two studies that have asked physicians to complete a specific scale rather than rely on perusal of case notes are more comparable with the current study, and have found that only 28% (Wilkinson *et al*, 1987) or 42% (Feldman *et al*, 1987) of psychiatric morbidity was detected. Even allowing for the fact that CIS classification is not error free, our results, although improved, confirm that physicians are missing much psychiatric pathology. The difference in detection for cases with low and high impact suggests that dermatologists were more likely to recognise psychological symptoms in those whose distress was related to skin pathology.

Does this matter? Our results suggest that 75% of the cases of psychiatric disorder in a dermatology clinic may be caused by or be closely related to skin disease. Indeed, it is possible that many patients are being referred to dermatologists as a result of that emotional distress rather than because of any feature of the skin disease. Such emotional disorder may require treatment in its own right, or may influence other decisions about treatment. We believe it is both unnecessary and inappropriate to refer all such patients to psychiatrists, and argue that our results suggest that physicians should be encouraged to become better skilled in the detection and management of these patients.

Implications

This paper attempts a classification of psychiatric disorder in attenders at a skin clinic. The principles behind the analysis may be valid in other medical settings with a similar high prevalence of psychiatric disorder, but where the separation of physical and psychological contributions to morbidity is more difficult. Future work is needed to determine whether each group has a different clinical course and response to treatment.

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Pervasive Developmental Disorders and Psychoses in Adult Life

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Of five patients with pervasive developmental disorders (PDDs), four developed psychotic illnesses in adult life. The other was treated with antipsychotic medication for many years following a mistaken diagnosis of schizophrenia.

Pervasive developmental disorders (PDDs) are a group of related disorders characterised by qualitative impairments in reciprocal social interactions and in non-verbal and verbal language, and by a restricted, stereotyped, repetitive repertoire of interests and activities. The abnormalities are 'pervasive' in the sense of affecting the individual's functioning in all situations. In most cases development is abnormal from infancy or early childhood. The term was used in DSM–III (American Psychiatric Association, 1980) and has been included in the draft guidelines for ICD–10 (World Health Organization, 1988) to encompass the spectrum, or continuum (Wing, 1988), of autistic disorders. Current classifications are largely untested and in many respects unsatisfactory.

The term 'Asperger's syndrome' has been used to describe a disorder in which children or adults have autistic impairments in social interaction and imaginative activities, but show more appropriate syntactical speech than people with Kanner's syndrome, and may not be so socially aloof (Wing, 1981). Wing (1986), while agreeing that no sharp distinction can be drawn between higher-level autism and Asperger's syndrome, commented:

> "One result of the publicity given to Asperger's work is a small but continuing series of referrals from psychiatrists working in the field of adult mental illness who have recognized the behavior pattern Asperger described in patients who presented diagnostic puzzles or had been called schizophrenic or obsessional."

Tantam (1988) has suggested that the concept of Asperger's syndrome should not be over-extended, and should be reserved for autistic children who use language freely but do not tailor its use to the social context, who wish to be sociable but fail to make relationships with peers, who are conspicuously clumsy, and have engrossing idiosyncratic interests and marked impairments of non-verbal expression. Neither DSM–III nor ICD–9 (World Health Organization, 1978) described this subtype of PDD, although DSM–III described 'schizoid disorder of childhood or adolescence', which had many similarities. The proposed ICD–10 describes five specific subtypes of PDD, one of which ('schizoid disorder of childhood') includes Asperger's syndrome.

In this paper we have used the classification of PDDs adopted in DSM–III–R (American Psychiatric Association, 1987), which describes two subtypes of PDD: autistic disorder, and pervasive developmental disorder not otherwise specified (PDDNOS). DSM–III–R also describes schizoid and schizotypal personality disorders and states that "The diagnosis of Autistic Disorder preempts the diagnosis of these personality disorders. However, these personality disorders preempt the diagnosis of Pervasive Developmental Disorder Not Otherwise Specified". The diagnostic criteria for schizotypal personality disorder, however, include the statement "Occurrence not exclusively during the course of Schizophrenia or a Pervasive Developmental Disorder". Schizophrenia may be diagnosed as a complication of autistic disorder "only in the rare instances in which prominent delusions or hallucinations meeting the criteria for Schizophrenia can be documented. Schizophrenia, however, preempts a diagnosis of Pervasive Developmental Disorder Not Otherwise Specified". This statement presumably refers to the differential diagnosis of disorders occurring in childhood, and does not preclude the diagnosis of schizophrenia occurring later in life in someone with a pre-existing PDDNOS. ICD–10 does not appear to take this hierarchical approach to diagnosis. (See Table I for a list of the relevant diagnostic categories in the two classifications.)

We describe five people with PDDs. Although they had a language disorder, they were able to give some account of their subjective experiences and behaviour. Four developed a psychotic disorder which led to psychiatric referral in early adult life. The fifth was incorrectly diagnosed as having schizophrenia because of his eccentric behaviour and a family history of the illness. In all cases, information concerning the developmental history

TABLE I
Diagnostic categories listed in DSM–III–R and in the proposed ICD–10

DSM–III–R	*Draft ICD–10*
Pervasive developmental disorders (Axis II)	*Pervasive developmental disorders (F84)*
299.00 Autistic disorder (Infantile autism, Kanner's syndrome)	F84.0 Childhood autism
299.80 Pervasive developmental disorder not otherwise specified	F84.1 Atypical autism
	F84.2 Childhood disintegrative disorder
	F84.3 Hyperkinetic disorder associated with stereotyped movements
	F84.4 Schizoid disorder of childhood
	F84.8 Other
	F84.9 Unspecified
Personality disorders (Axis II, 11 specific types described in three clusters)	*Abnormalities of adult personality and behaviour (F6, eight specific types described*
301.20 Schizoid personality disorder	F60.1 Schizoid personality disorder
301.22 Schizotypal personality disorder	
301.90 Personality disorder not otherwise specified	F60.8 Other
	F60.9 Unspecified
	F61 Mixed and other personality disorder
	F68 Other disorders of adult personality and behaviour
	F69 Disorders of adult personality and behaviour, unspecified
DSM–III–R provides a multi-axial diagnostic system, with the following axes	*A multi-axial system of diagnosis is being developed for ICD–10*
Axis I Clinical syndromes and V codes	
Axis II Developmental disorders and personality disorders	
Axis III Physical disorders and conditions	
Axis IV Severity of psychosocial stressors	
Axis V Global assessment of functioning	

was obtained by interviewing relatives or carers and from case notes. In case 4 most of the information used to make the diagnoses was obtained from the patient's relatives.

Case reports

Case 1: PDDNOS (Asperger's syndrome) and delusional disorder (persecutory type)

A is aged 18 years and the elder of two brothers. His mother suffered from hypertension in pregnancy. After 37 weeks he was born with a weight of 2.61 kg. He was nursed in a special-care unit for several days. In early life he was described as placid and slow to feed, failing to smile responsively or make eye contact. A convergent squint was noted at the age of 9 months, and an umbilical hernia was repaired at 12 months. A walked at 14 months, spoke his first words at 16 months, and used sentences around the age of 3. He was continent by the age of 3 years 6 months, and at this age had a single febrile convulsion. He was very anxious on starting school at the age of 4 years 6 months. Orchidopexies were carried out when he was aged 7 and 8 years. When he was aged 8 a test with the Revised Wechsler Intelligence Scale for Children (WISC–R) gave a full-scale IQ of 68 (verbal scale 71, performance scale 71). He was transferred to a special school at the age of 11, where unusual preoccupations and rituals (such as kissing his pencils and books in a set order before starting work) were noted. His educational progress was slow. He was clumsy in performing fine movements, and had a lumbering gait. At the age of 13 he was noted to be isolated at school and to have very poor social relationships with his peers. At the age of 16 he was transferred to a special class in a normal secondary school, where he became increasingly distressed and isolated.

He presented as a psychiatric emergency at the age of 17, in a state of intense anxiety which was secondary to the false belief that his father would be sent to gaol for non-payment of an electricity bill. He also believed, unshakably, that television programmes accusing him of homosexuality were being broadcast and that his grandmother had died, and he also thought that he might have AIDS. His appetite, weight and sleep pattern were unaffected and there was no diurnal variation in symptoms. Initially an organic condition was suspected, but extensive investigation, including blood count, biochemical profile, amino-acid chromatography, chromosome analysis, EEG, and computerised tomography (CT) of the head did not show any abnormality. An Axis I diagnosis of delusional disorder and supplementary diagnoses of Asperger's syndrome (meeting DSM-III-R criteria for PDDNOS) and mild mental retardation were made. Treatment with trifluoperazine and propranolol (to control anxiety) resolved the delusional state and he gradually improved. At follow-up 18 months later he was successfully attending a weekly residential school for autistic children, where he had made good progress, although he remained socially isolated, with ritualistic preoccupations and odd ideas, but no delusions. He is currently receiving trifluoperazine (2 mg b.d.) and propranolol (10 mg b.d.).

Case 2: PDDNOS (atypical autism) and psychotic disorder NOS

B is a 44-year-old man. The youngest of three siblings, he was born after a normal pregnancy and delivery. He walked at 18 months, became continent at 3 years 6 months, and at this age also started to talk. He was very withdrawn and anxious and cried excessively in early childhood. He played alone, and would not interact with other children. He attended school between the ages of 5 and 15. While at school he developed circumscribed interests in bus numbers and routes and car registration numbers, which he memorised. He played with toy cars by arranging them in straight lines, and collected key rings and watch straps, which he positioned on his desk in a set order. He worked in a bakery between the ages of 15 and 27, with supervision from his aunt. His aunt then changed jobs, and shortly afterwards B refused to go to work. He developed fears of stairs and heights, and was seen by a psychiatrist, who diagnosed a depressive illness and prescribed amitriptyline, with a good response. Wechsler Adult Intelligence Scale (WAIS) testing showed a full-scale IQ of 44: verbal 50, performance 43. He was referred to the mental handicap service. He had three further episodes of mental illness between the ages of 30 and 33. The first was characterised by the beliefs that a coach driver had paralysed his legs and that an ambulance driver had removed his shirt buttons; the other two were characterised by overactivity, reduced sleep and distractibility, but without persistently elevated, expansive or irritable mood.

He is now 44, and the most recent episode has consisted of 4-week to 6-week cycles of overactivity, overeating, stealing other patients' property and smearing faeces; alternating with 2-week to 3-week periods of withdrawal, mutism and catatonia. Investigations including blood count, biochemical profile, thyroid function tests, serum B12, serum folate and chromosome analysis were within normal limits. A CT scan showed moderate cortical atrophy with prominence of the third and lateral ventricles and slightly widened sulcal margins. A diagnosis of bipolar disorder was considered during the acute phase of B's illness, but the absence of a prominent abnormality of mood has led us to make an Axis I diagnosis of psychotic disorder NOS and additional diagnoses of PDDNOS and moderate mental retardation. B was treated with haloperidol and amitriptyline with little response, but responded well to treatment with electroconvulsive therapy (ECT) and lithium. He attended a pre-discharge rehabilitation unit, but other patients were unable to tolerate some aspects of his behaviour (in particular, repetitive stealing from their lockers), and he has subsequently returned to hospital. At follow-up one year after the most recent psychotic episode, he remains well but continues to be preoccupied with his previous circumscribed interests, especially wrist-watches.

Case 3: PDDNOS (Asperger's syndrome) and schizophrenia (undifferentiated type)

C is a 20-year-old man. An only child, he had a birth weight of 2.92 kg after an uneventful pregnancy and delivery. He walked at 13 months, but did not speak until he was over 4 years old. He was anxious and isolated at school, had no close friends, and was picked on because of his withdrawal and abnormal speech, which was monotonous and poorly enunciated. He also tended to omit part of sentences, and did not use gesture. C performed poorly at school (although he was noted to have good rote memory) and he was transferred to a special school. He spent his evenings writing out exact copies of the same few pages from a school book. He was clumsy in performing fine motor tasks and was preoccupied with wrist-watches, sometimes examining someone's watch, rather than their face, on first meeting them.

At the age of 15, while on holiday with his parents, he became very agitated, and kept saying that "everything has changed". He dangled coat-hangers out of the caravan window "to pick up signals", said that the microphones in a discothèque were telling him to dance, and believed that his watch had developed special powers. He was admitted to an adolescent unit, where a diagnosis of schizophrenia was made. He was treated with oral and depot antipsychotics, and made a slow but complete recovery.

At the age of 19, again while on holiday, he complained of feeling unwell and said that someone was following him, and that the IRA were planting loudspeakers in the caravan to listen to him. He was admitted to hospital. C believed that the telephone sockets in the hospital were observing him, that someone was using electricity to make his arm go hot and cold, and that he was being controlled by peoples' watches. He was on some occasions also overactive and disinhibited, and repeatedly left the ward to urinate over cars parked outside the hospital. Diagnoses of schizophrenia and a pervasive developmental disorder (subsequently classified as PDDNOS) were made, and he was treated with antipsychotics and lithium.

The schizophrenic illness remitted completely after approximately 15 months of treatment, and C was then able to attend adult literacy classes and a psychiatric day hospital, where he managed to achieve a reasonable degree of integration into some of the social activities. After a few months of attendance as a day patient the schizophrenic illness returned, and C was readmitted to hospital.

Case 4: Autistic disorder and major depressive episode

D, a 23-year-old man, lives with his parents and 26-year-old brother. He was born with a weight of 3.8 kg after an induced labour, 24 days after the expected date. He suffered the usual childhood illnesses and at the age of 4 months was admitted to hospital for 48 hours for treatment for an infection and lymphadenopathy; he has also suffered from eczema from infancy onwards. D started to walk at a much later age than his siblings and did not start to talk until he was 7. His mother thought he was deaf, but audiometry showed his hearing to be normal. He did not laugh or cry during childhood, and disliked being cuddled. He did not smile at people, and would not play or interact with his siblings or other relatives. He often walked out of the room if someone else came in. He played with cars by arranging them in lines, never pretending that they were cars. At the age of 10 he built a model of 'the airport of the future' from Lego bricks; it consisted of a pyramid with a rectangular base and layers of bricks, each layer being inset from that below by one brick in each direction. If routines were varied he lost his temper, and he had to have the same meal on the same day of the week. His mother once had her hair style changed to a much shorter one; until it grew back to the usual length he refused to accept that she was his mother. He did not reverse pronouns when speaking, but used words rather than sentences and often repeated words several times. He attended a special school, and until his recent illness attended an Adult Training Centre daily.

About 6 months before referral D began to behave oddly. He seemed to be miserable and was also irritable, losing his temper much more than usual. He refused to attend the ATC and spent all his time at home, wandering up and down stairs, walking in circles and humming, or staring out of the window. He neglected his appearance and personal hygiene and lost all interest in his war comics and computer games. He asked his mother to burn two sets of the *Encyclopaedia Britannica* because "they are dirty", and repeatedly said that a tree in his neighbour's garden should be cut down. For the first time in his life be began to laugh and cry, for no reason apparent to his relatives. Over the month before referral he had been eating very little and sleeping poorly, often getting up in the night to wander round the house. In the week before he was seen by a psychiatrist he had been smelling any food offered to him, often refusing to eat because "it's junk food".

When seen at home he was dishevelled and agitated. He sat staring in the opposite direction to the interviewer and would only reply to questions by saying "yes", "no", or "don't know". An Axis I diagnosis of major depressive episode and supplementary diagnoses of autistic disorder and mild mental retardation were made. Amitriptyline (150 mg at night), together with chlorpromazine in doses of up to 100 mg q.i.d. were prescribed. Shortly after starting treatment D said he wanted to kill himself, but at his and his family's request he continued to be treated at home. The depressive episode remitted completely after 3 months of treatment.

Case 5: PDDNOS (Asperger's syndrome) mistaken for schizophrenia

E, a 28-year-old man with one younger half-sister, was born after a normal pregnancy and delivery. He was hypotonic and extremely anxious in early childhood. His motor and speech development were slow, but exact details are not known. Psychological testing at age 5 showed an IQ of 74 (Terman-Merrill). He did not talk to, or play with, other children, moaned when he was talked to, and would only talk to adults with his hand in front of his mouth. He attended a special school, where school reports described him as timid and fearful, with abnormal preoccupations concerning trees and electricity pylons. He walked on tiptoe, and had such a peculiar skipping mannerism that his teacher recalled it vividly many years later.

Psychometry at age 11 showed a full-scale IQ of 69 (WISC). He produced detailed and heavily shaded drawings, which often omitted part of the subject. At the age of 13 he was referred to a paediatrician because of motor clumsiness. He had long, thin fingers, but no other specific abnormalities were found. Investigations, including chromosome analysis and amino-acid chromatography, were normal. E was seen by a child psychiatrist, who noted his preoccupation with science fiction, television programmes and space travel, concluded that he was a boy of limited intelligence who had a schizoid personality, and recommended that attention should be focused on his artistic talent, which was considerable.

When E was 14, his mother was admitted to a psychiatric hospital and found to have a paranoid schizophrenic illness. E was transferred to a residential school, where a medical report described him as timid and obsessional, with bizarre mannerisms. At the age of 14 years 6 months he was described as a "withdrawn, non-aggressive type of early schizophrenic" and treated with fluphenazine, which he has continued to take for 13 years. He continued to be preoccupied with space travel and electricity pylons, which he drew in great detail.

His most recent psychiatric contact was at the age of 27. He went to a social services hostel with a plastic milk bottle pinned to his lapel, and said it was his "other head". He was thought to be deluded, but an urgent psychiatric assessment found that E was still preoccupied with science fiction television programmes, including one featuring a character with two heads, whom he was emulating. He was not deluded, and had no other symptoms of psychotic illness. His social responses were abnormal; he stared fixedly at the interviewer for minutes at a time and used no gestures. His speech was monotonous, with a marked articulation defect. He repeated most sentences twice, omitting parts, and talked enthusiastically about science fiction programmes, having few other interests. Identical clocks, posters, and other objects were arranged symmetrically about his flat. These features, and the developmental history, were considered compatible with a diagnosis of PDDNOS, rather than schizophrenia.

Discussion

The relationship between autistic disorders and schizophrenia and other psychotic disorders is a matter of continuing debate. There are similarities to the evolution of the concept of childhood disintegrative disorder, as described in the proposed ICD-10. Children with this condition develop normally before losing previously acquired skills, such as speech and language, and developing a severe behaviour disorder. The condition may be a manifestation of a neurological condition and may be progressive (as in San Fillipo syndrome) or non-progressive (as in Rett's syndrome) (Corbett, 1987). Patients who appear to have suffered from childhood disintegrative disorder were described by de Sanctis (1906), who used the term 'dementia praecocissima', and who regarded the disorder as a very early manifestation of schizophrenia. Further cases were described by Heller (1930; translated by Hulse (1954)), leading to the eponymous term 'Heller's syndrome'. The description of children with autism by Kanner (1943) paved the way for the subdivision of the severe psychiatric disorders of childhood (childhood psychoses) according to their clinical features and natural history, added insights being provided by epidemiological and genetic studies. Malamud (1959) showed that the term 'Heller's syndrome' tended to be used as a label for a variety of organic brain disorders in patients presenting with psychiatric symptoms in childhood. He suggested that the term should be abandoned because it was imprecise and often confused with childhood schizophrenia. ICD-9 used the term 'disintegrative psychosis', and stated that the disorder may be associated with overt brain disease. Corbett *et al* (1977) described two patients (one with metachromatic leucodystrophy and the other with sudanophilic leucodystrophy) who developed progressive childhood disintegrative disorders. One boy was treated for a non-specific conduct disorder for several years, but at the age of 11 developed a psychotic condition and attacked his mother in response to third-person auditory hallucinations. The concept of childhood disintegrative disorder has therefore evolved from an initial era when it was regarded as an early form of schizophrenia, through a period in which it was distinguished from schizophrenia and from other childhood psychiatric conditions, to the current realisation that it is a useful description for a pattern of behaviour (often found in association with neurological disorders) which is sometimes accompanied in the later stages by symptoms found in psychotic disorders (including schizophrenia).

Similarly, Kanner (1949) initially stated that:

> "Early infantile autism may therefore be looked upon as the earliest possible manifestation of childhood schizophrenia. . . . I do not believe that there is any likelihood that early infantile autism will at any future time have to be separated from the schizophrenias, as was the case with Heller's disease or with many instances of so-called dementia praecocissima of de Sanctis."

The current concept, however, is of autistic and schizophrenic disorders being separate and unrelated (Kolvin *et al*, 1971; Rutter, 1974). This dichotomy has been reflected in some diagnostic criteria, including those of DSM-III. We agree with the statement in DSM-III-R that:

> "Though some early investigators suggested that these disorders were continuous with adult psychoses (e.g., Schizophrenia), substantial research suggests that they are unrelated to the adult psychoses. For that reason, and the difficulties of assessing psychosis in childhood, the term *psychosis* has not been used here to label this group of disorders: Pervasive Developmental Disorders is used because it describes most accurately the core clinical disturbance in which many basic areas of psychological development are affected at the same time and to a severe degree. . . . Other mental disorders, such as Major Depression, may occur during adolescence and adult life. They are most easily recognized in people who have sufficient speech to describe symptoms accurately."

Four of the patients described above developed psychotic illnesses. There have been other reports of people with autistic disorders who developed psychoses in adult life. Darr & Worden (1951) described a 33-year-old woman who had initially presented in 1921 at the age of 4. The clinical features recorded at that time enabled the authors to make a retrospective diagnosis of early infantile autism. As a child she avoided eye contact, was echolalic and averse to playing with other people and was preoccupied with shiny objects. In early adult life she lived according to a set of routines, and would fly into a temper if she was delayed in a theatre queue or if chicken was served without currant jelly. She was interested in music and Spanish, and learned to speak Spanish fluently. She had a few acquaintances, but tended to embarrass them through her repeated social blunders, such as stripping to the waist while on a walk with a group of people of both sexes, subsequently being enraged when her companion insisted that she replace her blouse. At the age of 29 she developed a respiratory infection and became deluded. After saying that her medication was poisoned and that she was urinating cider she was admitted to a psychiatric hospital. She appeared depressed and expressed various other delusions, including the belief that she contained chemical poisons and would explode if a match was struck, killing everyone in the building. At one point in her illness she became almost mute and had a shuffling gait. She was treated with deep coma insulin therapy, ECT and psychotherapy. It is possible that Darr & Worden's patient had Asperger's syndrome (PDDNOS) and that the psychosis was an affective disorder. Reiser & Brown (1964) described 125 children with 'infantile psychosis', nine of whom developed symptoms of psychotic illness in adolescence or adulthood. The diagnosis made by the authors was schizophrenia: "They showed a variety of features approximating the classical picture of chronic schizophrenic reaction of the paranoid type, with delusions of persecution, ideas of reference, notions of grandeur, and hallucinations". Dahl (1976) found that, of 17 patients initially diagnosed as having 'infantile psychosis', six later had a diagnosis of schizophrenia and three a diagnosis of atypical psychosis. The diagnoses of the clinicians looking after the patients were recorded, and the diagnoses of schizophrenia may be questionable in some cases:

> "The six schizophrenic patients were all described as autistic with bouts of temper, sometimes alternating with apathetic periods, hallucinations, and bizarre behaviour, ritualistic with stereotypies. Low intellectual function was described for some of them. Only a few have had delusions, perceptions (*sic*), and bodily hallucinations."

Wolff & Chick (1980), reporting 10-year follow-up of 22 boys with 'schizoid personality', found that nine had current psychiatric symptoms. Two had marked depressive symptoms (suicidal thoughts, hopelessness, poor concentration and early morning waking), one had dramatic mood swings, five had attempted suicide and ten had had suicidal thoughts since the age of 14. One patient (possibly two) had had a schizophrenic illness. Wing (1981) reported a high prevalence of superadded psychiatric illness in her series of 18 patients with Asperger's syndrome aged 16 and over, but cautioned that samples presenting to psychiatrists will necessarily be biased towards individuals with additional psychiatric disorder. Of the 18 patients, four had had an affective illness, four had become increasingly odd and withdrawn, one had an unclassified psychosis with delusions and hallucinations, one had had an episode of catatonic stupor and one an unconfirmed diagnosis of schizophrenia. Two patients had attempted suicide and one had talked of doing so. Petty *et al* (1984) carefully documented three children with infantile autism who developed symptoms of schizophrenia in childhood or adolescence. Symptoms included thought disorder (incoherence, loosening of association, illogicality, poverty of speech) accompanied by blunted or inappropriate affect; thought broadcasting, insertion or withdrawal; delusions of being influenced or controlled; somatic, grandiose, religious, nihilistic, or other bizarre delusions; auditory hallucinations; fusion of reality and internal mentation; and alterations of perception. Komoto *et al* (1984) reported two adolescents who had both infantile autism and an affective disorder (a 13-year-old boy with a bipolar illness and a 13-year-old girl with unipolar depressive episodes). Gillberg (1985) described a young man with Asperger's syndrome and a family history of bipolar (manic–depressive) disorder who had recurrent episodes of lethargy from the age of 8 years onwards, with a marked worsening following puberty. The episodes reached psychotic intensity, with apathy, depression, pervasive loss of interest, negativism and regression of self-help skills lasting between 14 and 17 days. Gillberg diagnosed manic–depressive psychosis and started treatment with lithium. Szatmari *et al* (1986) described a woman with Asperger's syndrome who developed auditory hallucinations (consisting of two voices talking about her or a single voice making disparaging remarks) in early adult life. Tantam (1988) has suggested that there is a particular association between Asperger's syndrome and the subsequent development of affective disorders.

Several authors have suggested a link between certain personality abnormalities and the subsequent development of schizophrenia (Essen-Möller, 1946; Nannarello, 1953) and other psychotic disorders (Langfeldt, 1953).

> "Shortly after Kraepelin first announced his concept of dementia praecox in 1896, he indicated that certain types of children seem predisposed to the condition and that in some cases the adult symptomatology could be traced back to early childhood. He noticed from the reports of others as well as from his own observations that some patients with dementia praecox, especially males, had the history of a quiet, shy, docile, retiring disposition in childhood, with no ability to make friendships or to live outside themselves." (Nannarello, 1953)

This 'schizoid' personality type shares some characteristics with the PDDs. Wolff and co-authors have used the term 'schizoid personality' to refer to children with a disorder indistinguishable from that termed 'Asperger's syndrome' by others (Wolff & Barlow, 1979; Wolff & Chick, 1980; Wing, 1981). Similarly, there have been suggestions that disorders resembling PDDs may occur among the relatives of people with schizophrenia. Rutter (1985) noted that personality abnormalities known to be genetically linked with schizophrenia were similar in some respects to Asperger's syndrome. Kerbeshian & Burd (1986) suggested that the criteria defining the personality disorder found unusually frequently in the relatives of people with schizophrenia (Kendler *et al*, 1984) may include people with PDDs.

Although Asperger (1944, 1968, 1979; Van Krevelen & Kuipers, 1962; Van Krevelen, 1971) found that the development of schizophrenia was rare in people with the syndrome later given his name, it is now apparent that people with PDDs may develop psychotic illnesses in adolescence or as adults. Classifications of pervasive developmental disorders need to take account of the possibility of superadded functional psychoses.

DSM–III–R is an improvement on its predecessor in this respect, although in other respects it is unsatisfactory; PDDs are not considered in the section dealing with the differential diagnosis of schizoid and schizotypal personality disorders, and the classification of PDDs does not recognise childhood disintegrative disorders as discrete entities. DSM–III–R employs a hierarchical approach to the diagnosis of PDDs and adult personality disorders, although research has not established whether PDDs, schizoid personality disorder and schizotypal personality disorder are distinct diagnostic entities or extremes in a continuum (with pervasive developmental disorders of childhood at one pole and schizoid personality disorders diagnosed for the first time in adult life at the other). The proposed ICD–10 also has deficiencies, particularly the unclear distinction between adult and childhood schizoid personality disorders. Further research needs to be directed to the clearer definition of these disorders, and to the nature of their relationship with schizophrenia and other psychoses.

Until these relationships have been clarified we suggest that when the predominant clinical features are solely the avoidance of (or indifference to) social relationships and a restricted range of emotional expression, then a diagnosis of schizoid personality disorder should be considered. When abnormalities in social functioning develop in infancy or early childhood, and are accompanied by abnormalities of speech or the use of non-verbal communication (or by an inability to tailor the use of language to the social context), and by a restricted, stereotyped, idiosyncratic repertoire of interests and activities, then the diagnosis of a pervasive developmental disorder should be considered.

The patients described above illustrate an aspect of PDDs which is of particular interest for general psychiatrists; pervasive developmental disorders may be complicated by psychotic illnesses presenting in adulthood, or may be mistaken for them.

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Point of View

Is Your 'Double-Blind' Design Truly Double-Blind?

ALISON OXTOBY, ANGELA JONES and MICHAEL ROBINSON

Before a drug trial, researchers reasonably plan that participants will remain ignorant of which drug each patient is taking, reflected in the use of allegedly identical preparations. However, only rarely is this plan subjected to systematic scrutiny after the event, and our point of view is that this is unsatisfactory.

There are grounds for scepticism about the validity of the 'double-blind' design. Side-effects have been thought to be revealing (Letemendia & Harris, 1959; Leyburn, 1967; Rickels *et al*, 1969; Marini *et al*, 1976). Notionally identical preparations have been found to be distinguishable (Hill *et al*, 1976; Robinson, 1985). Patients have deliberately subverted the 'double-blind' design (Howard *et al*, 1982) perhaps because of an understandable wish to have the best treatment available (Zifferblatt & Wilbur, 1978). Guesses made by participants during the study have been significantly better than chance expectation (Rickels *et al*, 1969; Brownell & Stunkard, 1982; Byington *et al*, 1985).

Our own researches suggest that there is some resistance to acknowledging the problem. Of the 16 'double-blind' drug trials described in the *American Journal of Psychiatry* and the 12 appearing in the *British Journal of Psychiatry* in 1982, only one in each set included an attempt to test the 'double-blind' design using guesses: those by Brownell & Stunkard (1982) and Mawson *et al* (1982), respectively. The paper describing this unsatisfactory state of affairs was rejected by the *American Journal of Psychiatry* but accepted by the *British Journal of Psychiatry*. Of the nine 'double-blind' drug trials published in *Acta Psychiatrica Scandinavica* in 1985, only the one by the Sussex Clinical Trials Group tested the 'double-blind' design using guesses, and the paper wherein these findings were described was rejected. Again, in 1986, *Psychological Medicine* published an article by Dickson & Kendell describing how admission and readmission rates for mania, and also for depression, had risen steadily, when they should have fallen progressively had lithium been effective, which the authors regarded as proven by several 'double-blind' trials (Baastrup *et al*, 1970; Coppen *et al*, 1971; Prien *et al*, 1973, 1984). We reviewed these trials and showed that none of them had included systematic tests of the 'double-blind' design using guesses by the participants. Baastrup *et al* had in fact found lithium in the serum of four patients who had been given placebo, suggesting that the lithium and placebo tablets had been distinguishable. In the study by Coppen *et al* the assessor had had to record any guess that he made as to whether the patient was taking lithium or placebo and, having felt that he could only guess at the treatment of 13 out of the 65 patients, he was right in nine. However, an assessor's feelings are hardly a convincing basis for scientific rigour, let alone the prescription of a potentially toxic drug, and the 'double-blind' design would have been more completely tested had guesses been made for all the patients, regardless of how the assessor felt, and by all the patients. Both of the studies by Prien *et al* had included a change from active drug to placebo, so that a basis for comparison between them was inherent in the design; all the more reason for validation of the supposed 'double-blind' design, but there was none. These findings were presented in a paper that also showed that in none of the six 'double-blind' drug trials published in *Psychological Medicine* between November 1983 and August 1986 had guesses by the participants been used to authenticate the design. This paper too was rejected, the opening remark of one of the two reviewers being "The Luddites rise again!"

The present, seemingly cherished, system fails to distinguish between a drug that is truly superior, and one that can be made to appear so because it is identifiable through its side-effects, appearance, taste, or smell. To remedy this, at the end of every drug trial that has a 'double-blind' design, the participants should be asked to guess the patients' drug status, giving reasons, and then the guesses should be compared against chance expectation. If neither the patients nor the researchers guess significantly better than chance, then the likelihood is that the trial was truly double-blind and it can be presented as such. If, however, the guesses of either the patients or the researchers exceed chance expectation, then this claim cannot, and should not, be made. The trial was probably not double-blind, which raises the obvious question of why it was not, when recourse can be taken in the reasons given by the participants for their guesses. The results can then be reworked with the exclusion of those patients whose drugs were identified on the basis of side-effects, appearance, taste, or smell, and not on the basis of their therapeutic effect.

The measures delineated will provide prescribers with important information about what actually happened during a drug trial, as distinct from what was planned to happen: they may be of considerable heuristic value, which we hope to see discussed in the correspondence column. What is unequivocal is that the presumption that a plan to which one has aspired has come to fruition by virtue of aspiration alone is not science, and is particularly inapposite for a profession which should have a reputation for making clear distinctions between fantasy and reality.

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Brief Intermittent Neuroleptic Prophylaxis for Selected Schizophrenic Out-patients

H. A. McCLELLAND, G. HARRISON and S. D. SONI

"A study was conducted to investigate a novel approach to the prophylaxis of schizophrenic relapse. The treatment strategy comprised brief intermittent courses of neuroleptic agents begun as soon as non-psychotic symptoms believed to be early signs of relapse appeared. Fifty four stable, remitted outpatients meeting the American Psychiatric Association's DSM-III criteria for schizophrenia were randomised double blind to receive brief intermittent treatment with either active or placebo depot neuroleptic injections. Only three patients given placebo injections and two controls were admitted to hospital during one year of follow up. Eight (30%) of the patients given placebo injections and only 2 (7%) of the controls, however, had a recurrence of schizophrenic symptoms. Patients given placebo injections experienced fewer extrapyramidal side effects and showed a trend towards a reduction in tardive dyskinesia. Dysphoric and neurotic symptoms were identified before eight out of 11 relapses, and these symptoms were more frequent in patients given placebo depot injections. These results suggest a viable but not necessarily better alternative to continuous oral or depot treatment for less ill, chronic, stabilised schizophrenics based on the early treatment of putative prodromal symptoms of relapse."

The summary quoted above is from an article by Jolley *et al* (1989). The present authors were invited to comment upon the study.

H. A. McClelland

Neuroleptic medication is an indispensable evil in the treatment of schizophrenia. Indispensable because even though there is no evidence that these drugs have increased the 'cure' rate of schizophrenia, their beneficial effects on relapse rates and control of symptoms cannot be disputed; evil because of the wide range of side-effects that can be displeasing and even a source of hardship for the patient. Understandably but unfortunately, psychiatrists have pursued the Holy Grail of achieving at all costs the maximum possible antipsychotic effectiveness of these drugs. There has been an acceptance of a loosely defined standard dosage, with frequent recourse to above-average dosage in treatment-refractory patients, although if a steady increase in dosage does not cause the desired effect, it is fairly uncommon for the dosage to be reduced. The outcome is a range of adverse reactions to which the psychiatrist is more tolerant than the patient.

Early attempts at overall low dosage, by instituting 'drug holidays' with fixed and arbitrary intervals, all failed, but the recent upsurge of interest in continuous low-dosage or intermittent neuroleptic regimes has been carried out with more sophisticated and carefully supervised studies. It is no coincidence that systematic trials of these procedures have been performed initially in the USA. There, the increasing awareness of tardive dyskinesia and of the misery caused by side-effects in general has been forcibly drawn to the attention of psychiatrists by the vociferous advocates of patients' civil rights, accompanied by costly legal actions.

The trial by Dr Jolley and his colleagues is admirable in concept and design. That relapse is frequently preceded by dysphoric symptoms is confirmed. The overall reduction in side-effects is clearly shown, and this must increase the patient's co-operation. Some years ago, Van Putten (1974) showed that many patients were not so much non-compliant as partially compliant, in that they self-medicated at a dose level which made their side-effects bearable. Yet if a doctor does not know how much medication a patient is taking, treatment becomes a blind-man's buff.

The authors do not claim that all patients are suitable for their regime, and indeed accepted only 40% of the patients referred. They delineate certain obvious criteria for inclusion, such as lack of dangerousness in relapse and reasonable degree of pre-trial stability. This drug regime is therefore not suitable for the majority of patients with chronic schizophrenia. This agrees with a recent study (Chiles *et al*, 1989) on eligibility of patients for intermittent medication, where the authors found that only one-third (34.8%) of chronic schizophrenic patients attending a mental health centre were suitable.

In all drug trials, there is a risk that a small but distinct subgroup can be overlooked. For some patients, a relapse can have serious consequences for livelihood and domestic stability. There is also a small proportion who may have a number of relapses followed by excellent remission, but then a further relapse leads to a serious defect state. Ciompi (1980) estimates that such an outcome occurs in about 10% of patients. One cannot predict which patients belong to the subgroup, and although the relapsed patients in the Jolley trial did well with early intervention, this might not be true for all relapses over a longer period of time.

The duration of follow-up is critical in the evaluation of any management regime. Some early trials of low-dose medication were for less than a year, and even a trial of one year may not be sufficient. The relapse rates in ultra-low and standard dosage in the study by Marder *et al* (1987) were similar over one year but over two years, the rate on ultra-low dose was very much higher, although if the psychiatrist could alter dosages, the relapse rates were similar.

In the Jolley trial, the results over a year were acceptable, even if those on intermittent dosage did show more dysphoric symptoms and more relapses. However, if the study had been continued for a further year, deterioration of those on intermittent medication may have been unacceptable in terms of frequency and severity of relapse. The authors have properly argued that a similar trial on intermittent medication by Carpenter *et al* (1987) did not show any appreciable difference in the two groups over two years. Another recent trial (Hogarty *et al*, 1988) of continuous low dose (but not ultra-low dose) also did not show any differences in relapse rates, compared with a standard dose.

However, there is an important maverick study on continuous low dosage from Manchester (Johnson *et al*, 1987). Not only did those investigators find a significantly increased relapse rate at 12 months, comparing standard with reduced doses (50%) of flupenthixol decanoate, the relapse rate increasing to 56–75% over two to three years in the reduced-dose group, but the latter experienced neither improvement in social functioning nor reduction in side-effects (apart from tardive dyskinesia). The patients in this trial were stabilised out-patients, but they were entered consecutively, and could well have been less symptom-controlled than those in the Jolley trial. Assessments were carried out at three-monthly intervals, and this trial reflects more accurately the conditions of day-to-day clinical practice.

On balance, it would seem that with judicious selection of patients, the intermittent medication and other low-dose (but not ultra-low) techniques can be a significant advance in the treatment of a *minority* of patients with schizophrenia. Jolley *et al*, like most other investigators, have emphasised the fewer side-effects, with the patient having a better quality of life overall. Such results have been obtained by enthusiastic and experienced workers after lengthy assessment (and presumably supportive) interviews with the patients at monthly intervals, and there were educational packages for patients and relatives. Chronic patients with functional psychosis (whether in good or incomplete remission) require such meticulous and frequent supervision so that modern drug, social, and counselling techniques are properly utilised. This will include the development of case registers and continuity of contact with interested therapists. It is clear that these ideal conditions do not exist in real life, except in a few centres with special resources, and they are very difficult to maintain over the long periods necessary in the management of schizophrenics.

For some years, I have endeavoured to reduce medication in my patients and am in no doubt that many do very well on smaller amounts than what are usually regarded as 'standard' doses. However, until I have enough resources to organise a fool-proof community service, my preference remains for constant low dosage in carefully selected and monitored patients, rather than "intermittent neuroleptic prophylaxis", which requires a very efficient service indeed. Whatever one's choice, though, the present stereotyped drug regimes administered to all patients cannot be the best clinical practice.

G. Harrison

Throughout the history of medicine, from blood-letting to aggressive cytotoxic therapy, there have been examples of cures which may be worse than the illness being treated. While the side-effects associated with neuroleptic treatment fall far short of equivalence with the distressing personal and social sequelae of unremitting psychosis, the authors remind us of the price sometimes paid for effective prophylaxis. Graphic imagery of the "greasy masked facies, stooped posture, 'dancing feet' and slow, shuffling gait" which "mark some patients out in the crowd" readily engages our interest in any treatment approach promising effectiveness while reducing the cost to the patient.

In parallel with the search for new groups of drugs having intrinsically fewer side-effects, there have been a number of alternative strategies suggested for the delivery of those already in use. These have included low-dose regimes, 'drug holidays' and, most recently, brief intermittent therapy.

This is an important and carefully executed trial of a variation of brief intermittent treatment. The strategy proposed in this paper relies upon identifying a "personal style of relapse" in individual patients, characterised by the emergence of non-specific neurotic or dysphoric symptoms before relapse. Oral haloperidol is then rapidly introduced in order to prevent psychotic symptoms becoming fully established.

The authors are to be commended on their detailed and careful presentation of their findings. They candidly describe this as a study of "selected schizophrenic patients". As in many intervention studies, the subjects bore little resemblance to the majority of patients currently maintained in our clinics. In effect, they were patients who had complied with depot neuroleptics for six months before entry (and who therefore had residual blood levels during the trial), who had been stable and free of symptoms over this period, and in whom relapse had not previously entailed definite risk to self or others. Of those passing the provisional filter of referral by clinicians who thought that they might benefit from the treatment, only 40% were entered for the study. The intervention group had a higher age of onset of illness, suggesting a better prognosis overall.

At one-year follow-up, 76% of the study group had had prodromal symptoms (non-specific neurotic and dysphoric complaints), compared with only 27% in the continuous depot control group. Thirty per cent relapsed, of whom half were apparently withdrawn from blind conditions because they were either ill for more than eight weeks or had experienced two or more relapses in six months. In contrast, only 7% of the control group relapsed, although there was little difference in the need for hospital admission or in use of compulsory powers. Advantages to patients in the study group included fewer extrapyramidal side-effects, as well as a trend towards a reduction in tardive dyskinesia.

Despite the lower incidence of side-effects, the actual benefit to patients in the experimental group is difficult to quantify. Prodromal symptoms involved real suffering to patients and, following the educational package about their illness, they knew that these carried the threat of impending psychosis. While those in the study who relapsed did not usually require hospital admission, the repercussions in less compliant, less carefully selected, and less closely supervised patients in our clinics require little imagination.

To show a true advantage, a treatment package involving significantly more risk of relapse and a higher prevalence of non-psychotic symptoms must demonstrate substantially lower side-effects and longer-term advantages of improved social outcome. A week may be a long time in politics, but one year is a notoriously limited period for assessing the course and outcome of schizophrenic syndromes. The results in the second year of follow-up will demonstrate the true worth, or otherwise, of this treatment. By that time, residual depot medication will have completely cleared from patients in the intervention group, and the additional social support they required over the first year may undergo subtle changes in both its intensity and the novelty of its impact. We await follow-up data from this research team with interest. Until then, even my most 'selected patients' will remain on continuous medication.

S. D. Soni

The paper from Charing Cross Hospital, London, describes a 'novel' approach to neuroleptic prophylaxis in schizophrenia. The study has been carried out with rigorous attention to methodological detail, as reflected in its design, and has produced interesting results. Briefly, these suggest that in certain 'selected' patients, continuous maintenance neuroleptic therapy may not be necessary; instead, they could be carefully monitored following recovery from acute psychosis and at the first signs of imminent relapse, oral neuroleptics instituted for brief periods to control symptoms and abort a florid relapse. The study raises important issues both with regard to the assumptions on which the study is based and inferences drawn from the findings.

The idea of brief intermittent neuroleptic prophylaxis ('targeted pharmacotherapy') for relapse in schizophrenia was introduced because of concern about the adverse effects of long-term medication, especially the risk of tardive dyskinesia (Herz *et al*, 1982; Carpenter & Heinrichs, 1983). The approach involved establishing criteria for selection of patients, tapering of medication, careful monitoring for prodromal signs of exacerbation, and restarting medication if indicated by early signs of relapse (Chiles *et al*, 1989). The assumption behind this strategy is that in many schizophrenics, the relapse occurs in stages (Docherty *et al*, 1978; Herz & Melville, 1980) so that it might be aborted before the development of a florid psychotic state. Previous studies have confirmed that this is possible, but that it requires careful selection of patients (Herz *et al*, 1982). The patients selected for this study were stable schizophrenics on maintenance depot neuroleptics, but few other criteria are mentioned, except that the treating clinicians thought they would be suitable for the study. Chiles *et al* (1989) have in fact indicated specific exclusion criteria for their 'intermittent medication' regime, such as presence of baseline symptoms, current stressful life events, uncooperativeness, hospital admission in the previous three months, suicidal behaviour, use of other psychotropic medication, etc. Further research should crystallise these observations and establish firm criteria, so that the findings could be translated into clinical practice.

Pharmacokinetic studies on depot neuroleptics reveal a prolonged and variable elimination rate, especially for fluphenazine decanoate; this can be an important confounding variable which, quite appropriately, has been discussed by the authors but rejected as clinically insignificant. The abrupt withdrawal of fluphenazine decanoate in this report also differs from the design of other similar studies, which recommend gradual tapering of the therapy. Finally, patients included in this study were stable schizophrenics; it is, however, well established that follow-up of treated schizophrenics in the first 12 months after recovery from acute psychotic episode reveals much higher rates of relapse than follow-up of similar patients who have been stable for a year or more on maintenance neuroleptic treatment (Hogarty, 1984). The findings in the present study therefore may not be wholly applicable to patients who have just recovered from a clinical episode of acute psychosis.

An important factor in assessing the value of this study concerns the nature of relapse. A key assumption in it is that the non-specific symptoms which were seen in patients were in fact early signs of schizophrenic relapse, but this is by no means established. As the authors quite rightly indicate, schizophrenics often show dysphoric symptoms in response to adverse life events, which may or may not predict an imminent relapse. Many schizophrenics also continue to show intermittent or sustained affective and/or neurotic symptoms while on stable doses of neuroleptics, and it is imperative that the relationship of these symptoms to relapses is carefully investigated.

An aspect of clinical significance is both the immediate and long-term effects of relapses on the handicaps of schizophrenic illness. One reason for maintaining patients on neuroleptic therapy is to prevent distress to both the patient and his relatives which is caused by excacerbation of acute psychosis. This aspect may certainly be reduced, but never eliminated, in some patients with the use of brief intermittent therapy. In our choice of approach for individual patients, these factors may have to be carefully balanced. Another consideration is the uncertainty about the relationship between severity and frequency of relapses and the eventual emergence and severity of deficits (including negative symptoms). If such a relationship exists, then the benefits obtained by reduced exposure to neuroleptics by the brief intermittent therapy recommended by this study may well be outweighed by the development of a more severe defect state and the consequences this may entail for the functioning of the patient. These aspects certainly need further investigation.

A final point relates to cost-effectiveness: maintenance neuroleptic therapy is relatively inexpensive; continuous, careful monitoring of patients, on the other hand, requires much staff time and vigilance, as well as active involvement and education of relatives or carers. These factors need to be carefully evaluated, especially in terms of cost/benefit analysis before the strategy proposed could be generally accepted, since selection of patients and the long-term effects on schizophrenics of repeated (albeit abortive) relapses still require further investigation. Follow-up of the present cohort may clarify some of these points, and we look forward to further reports from this centre.

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Case Conference

Abnormal Involuntary Movements

BENJAMIN HUGH GREEN

The differential diagnosis of an athetoid arm movement in a 54-year-old lady with a psychiatric history of affective disorder was discussed. Further investigations after the conference yielded a firm diagnosis that unified both physical and mental symptoms.

Objective

This is a report of a special case conference at the Royal Liverpool Hospital on 28 November 1988. The conference was asked to examine a patient's physical symptoms in the light of her psychiatric diagnosis.

Presentation of case

Miss D, a 54-year-old, Roman Catholic, unemployed spinster was admitted to the Royal Liverpool Hospital in October 1988 following a consultant domiciliary visit. Her presenting complaints were of abnormal involuntary movements of her right hand and arm, racing thoughts, 'high' mood, and poor sleep. Two weeks earlier she had been complaining that she was depressed because of continuing involuntary movements of her right arm. At that time she stopped her maintenance medication of chlorpromazine, which she had been taking for over five years for bipolar affective disorder. She had previously discontinued her lithium prophylaxis in July 1988 because of worsening psoriasis, and because she felt that her thinning hair was attributable to lithium.

After she stopped the chlorpromazine she rapidly became elated. She became overactive and garrulous. Her sleep had reduced to four hours per night. Her appetite was poor and she was losing weight.

The involuntary movements of her right hand and arm had begun two years earlier. At first she noticed only small movements of the wrist and fingers, but these became gradually worse so that they eventually involved the whole arm and hand in athetoid movements. These increased with anxiety and improved if she was distracted or relaxed. On some days the movements would be worse than others. The athetosis could sometimes wake her at night. When sitting in a chair she would hold a table with her right hand in order to try to suppress the movement. Just before her admission she felt the athetosis was worse than ever before.

Psychiatric history

In 1977, when she was 42, Miss D was admitted to Rainhill Hospital for six months. The admission followed a series of arguments with her sister and half-sister. She had been rivalling her sister for the attention of her two teenage nephews, and had been interfering in the running of her sister's house, where she lived. After Miss D had searched through her sister's private letters to try to establish that the boys' mother was "unfit to care for them", a solicitor was consulted. In this atmosphere of increasing hostility, Miss D's behaviour became disturbed. She assaulted her half-sister and was admitted from casualty after presenting a mixed affective picture with agitation, low mood, some pressure of speech and flight of ideas, and ideas of guilt and persecution. She complained of "whispering noises" against her in her home.

On the ward she behaved in a variety of abnormal ways, usually at times when she knew she was being observed. She pulled other patients' hair, kicked doors, threw the fire extinguisher, and lay under her bed at night, saying the floor was "softer" than the mattress. She would stand silent and still for minutes holding a hatpin in one hand and a ball of wool in the other. She sang loudly in the evenings. When asked why, she replied, "because it's cheaper after six", a reference to a telephone commercial. On one occasion, when asked how many legs a horse had, she answered by getting down on all fours and whinnying.

For reasons that are not clear in the case notes, a diagnosis of hysterical conversion syndrome was made at that time and she was treated with multiple abreactions using diazepam. Miss D became so suggestible that she eventually would enter a deep trance if only 1 ml of distilled water was injected. Each abreaction focused on her feelings of loneliness and rejection by her sisters. It became clear that she had not mourned her father, who had died in 1972, and she began then to grieve for him. She was discharged well after six months and followed up for two years in the out-patients department on no medication. She remained well.

In 1983, when aged 48, she was admitted to the Royal Liverpool Hospital. Before her admission she had been ostracised by her colleagues at a city-centre department store for refusing to join a union. This, together with uncertainties over the store's future, had weighed heavily upon her. She presented with a history of poor sleep, low mood, tiredness, and aggression towards her half-sister. An initial diagnosis of reactive depression was modified when after one week she became elated, with pressure of speech and flight of ideas. She began overspending, and was interfering and restless. She sang when she had blood taken. She was diagnosed as having bipolar affective disorder and treated with chlorpromazine and lithium. She was discharged two months later on chlorpromazine (25 mg b.d. and 125 mg *nocte*) and lithium carbonate (800 mg *nocte*). There were no features of akathisia or dystonia noted then. She was maintained on varying combinations of these two drugs until 1988. In the follow-up clinic over these five years she was noted to become elated only twice, and these episodes coincided with a fall in her serum lithium.

Medical history

Apart from a groin abscess as a child and psoriasis from young adulthood her physical health was good until 1985, when she had a right mastectomy for breast cancer. She was given radiotherapy and tamoxifen. On admission her only regular medication was tamoxifen (20 mg b.d.).

Family history

Miss D's Roman Catholic mother died aged 42 of ovarian carcinoma, when Miss D was eight. At the time of her death her mother was pregnant with twins.

Miss D's Protestant father brought up the family's three children. He became a "father, mother and brother" to Miss D. He was a self-employed plumber. Miss D was conscious that he would have preferred her to have been a boy to act as his 'right hand man' in his business. He died of pneumonia in 1972 aged 85.

She had two siblings: an elder half-sister, N, aged 61, from her mother's previous marriage; and C, a sister aged 52, who had two illegitimate children. All the children were brought up as Catholics. The three sisters were very close, and lived together until 1965 when C became pregnant and had to leave the family home.

There was no psychiatric illness or similar movement disorders in the family.

Personal history

Miss D had a normal birth and was brought up in Liverpool. She had a normal, happy infancy, living with her father, mother, and two sisters. She had no neurotic traits. After her mother died, her father became her main emotional support. Miss D went to school during the war at two inner-city Catholic schools. Unlike many of her generation in Liverpool she was not evacuated. She left school at 15 with no qualifications and became a shop assistant for two years. At the age of 17 she joined the WRAF, "to prove to my father that I was as good as a boy. There had been generations of our family in the Army for 200 years." After this she spent 20 years as a stockroom supervisor for a chain store.

After 1970 she began to help her sister, C, look after her two illegitimate sons. Her father died in 1972. In 1977 she became 'overinvolved' with her two nephews and suffered her first psychiatric illness, but returned to work some six months later. She stopped work in 1983 when the store closed, and has since remained unemployed.

At menarche she was 12. Her half-sister N had already told her the 'facts of life'. From the age of 13 her sexual fantasies were predominantly heterosexual. Her main mode of sexual gratification was, and is, masturbation. Miss D's strict Catholic upbringing is reflected in the fact that at 53 she is still a virgin. However, she had been engaged three times, at 17, 19, and 38. Her first engagement lasted only a few months because she refused to have full sexual intercourse. Her second engagement, when she was 19, lasted ten years. Again, the relationship did not progress beyond foreplay, and the engagement ended when he suddenly married someone else. When she was 38 she became engaged for the last time, but this ended when her Protestant fiancé became a vicar. She nearly became engaged for a fourth time when she was 39. She wears a dress ring on the ring finger of her left hand, which she describes as a present to herself when she was 40. It looks just like an engagement ring. She has no boyfriend now.

Social circumstances

Miss D lives with her elder half-sister, N, in their jointly owned house, which is the family home in which she was born. The household is financially stable. Miss D smokes 200 cigarettes a week, but drinks no alcohol.

Pre-morbid personality

Miss D is normally said to be jolly, chatty, and 'bubbly'. She maintains an optimistic outlook on life, and rationalises her misfortunes away. She admits to being sensitive to criticism and sometimes lonely. In her work she was a conscientious perfectionist, and keeps this attitude in her housework, which is carried out according to a rigid routine. She still attends Mass regularly. She has few hobbies, and regards herself as the mainstay of the family. There is no evidence of pre-morbid cyclothymia.

Mental state examination

Miss D is a 54-year-old caucasian woman, who looks somewhat older than her years. Her hair is neglected and thinning but otherwise she is clean and tidy. Both hands have nicotine-stained fingers and cherry-red finger nails which she had painted herself to conceal psoriasis.

During the interview Miss D was co-operative and maintained excellent rapport. She was slightly agitated. Her right hand and arm were involved in gross athetoid movements.

As the patient relaxed through the interview the movements became less marked.

Objectively Miss D was cheerful to the verge of elation. She became tearful suddenly in the interview when discussing her late father. Subjectively she said her mood was normal for her. She was garrulous and difficult to keep to the point. Her speech was relevant but tended to circumstantiality.

The form of her thoughts was normal, but the content was dominated by her pre-occupation with the athetosis of her right arm. There was a slight grandiose flavour to her ideation – she believed that indirectly her admission for assessment would benefit "a great many people", but there were no overt psychotic features. She was cognitively intact and understood the purpose of her admission. She felt her athetosis was due to the chlorpromazine.

Physical examination and investigations

Miss D was a thin, elderly lady with a focal athetosis. Her hair was noticeably sparse. She had a conjunctivitis. There was a right mastectomy scar, but no evidence of recurrence at the site or lymphadenopathy.

There was no evidence of orofacial dyskinesia. A neurological examination was normal except for the athetosis, associated with weakness and increased tone. There was some incoordination with dysdiadochocinesia of the right hand.

A full blood count, urea and electrolytes, liver function tests, thyroid function tests, syphilis screen, chest and cervical spine X-ray, computerised tomography (CT), and EEG were all normal. There were autoantibodies to cell nuclei. Her serum copper level was mildly raised.

Course on admission

Miss D was re-started on her lithium, but not her chlorpromazine. Tetrabenazine was added to the lithium and tamoxifen. A month after admission, although the athetosis persisted, the patient reported a definite improvement in the movements. Her mental state was then normal and she had returned to her usual enthusiastic and chatty self. A neurologist saw her in hospital and diagnosed the condition as tardive dyskinesia.

Conference discussion

DR POOLE (*consultant psychiatrist and chairman*): This is a complicated case and several questions arise. I find it hard to accept the neurological opinion that this lady's abnormal movements are due to tardive dyskinesia; furthermore, the treatment of her psychiatric state and neurological problem interfere with each other. We must also bear in mind the significant psychological issues, particularly those of grief and loss.

To facilitate the proceedings, a possible differential diagnosis, produced at the time of admission, was presented for discussion. Five causes of the abnormal movement were put forward: tardive dyskinesia, a discrete lesion of the left basal ganglia, a secondary neoplasm, hysterical conversion, or some other systemic condition such as multiple sclerosis, Wilson's disease, or Huntington's chorea.

DR ABOU-SALEH (*senior lecturer in psychiatry*): As regards diagnosis this is undoubtedly a case of focal athetosis of the right arm, and although bipolar affectively ill patients are highly vulnerable to tardive dyskinesia, there is no evidence of tardive dyskinesia itself. The aetiology of this condition may or may not be related to exposure to long-term neuroleptic treatment: it may be a coincidental development, and this is more likely as it is unilateral and circumscribed and it is not associated with tardive dyskinesia. One should also mention, if only to dismiss it, the possibility of a cerebral tumour secondary to breast cancer. The CT scan was negative, but I wonder whether nuclear magnetic resonance with its higher resolution could show a small lesion?

As regards management, tetrabenazine is the most appropriate treatment, but this could complicate the management of the affective disorder: its powerful amine-depleting effects might precipitate a depressive relapse. Lithium appears to have been effective except for aggravating her psoriasis, and the alternative might be carbamezapine.

DR WILLIAMS (*senior house officer*): I notice from interviewing the patient that she has perfectly polished red nails which she has been able to do herself, using both hands in turn. She says she has always been able to control her hands to paint her nails, even when the movement was at its worse.

Tardive dyskinesia can fluctuate in its severity according to the patient's level of arousal: the patient might still have tardive dyskinesia and, when relaxed, be able to control hand movements enough to apply nail polish.

The commonest site for tardive dyskinesia is around the mouth and tongue, and this is absent in this patient. There is support for involvement of the trunk, arms, hands and legs forming a distinct subgroup of tardive dyskinesia (Kidger *et al*, 1980). The elderly are seen as being more vulnerable to developing tardive dyskinesia on neuroleptic medication and usually the form taken is that of a choreiform movement (Task Force on Late Neurological Effects of Antipsychotic Drugs, 1980). Recent work on the pathophysiology of the condition suggests that chronic dopamine blockade of striatal neurons produces altered activity in the striatonigral GABA pathway resulting in irregularities in GABA transmission from the basal ganglia (Thaker *et al*, 1987).

Tardive dyskinesia is however seen as a diagnosis of exclusion. Even when there is a history of prolonged neuroleptic administration, other causes of persistent movements should be ruled out (Munetz & Benjamin, 1988).

DR LOVETT (*lecturer in psychiatry*): I think Miss D's presentation may be due to multiple aetiologies, which need not be mutually exclusive. She may indeed have a bipolar affective diorder, but this does not exclude the possibility that the 'involuntary' movement of her right arm is the result of a hysterical conversion state. There is evidence in her past psychiatric history that she uses dissociative mechanisms to cope with stress. Alternatively the movements could be the result of hysterical elaboration of an organic condition which is yet to be identified.

There are suggestions in her psychosexual history and psychiatric history that hysterical behaviour is not uncommon in this lady, and perhaps hysterical elaboration is in keeping with her personality. Whether she has a full-blown hysterical personality disorder is more difficult to say, but of course a hysterical conversion state can occur in any personality type.

Miss D's hysterical conversion state was diagnosed in 1977, and six years later she was given a different diagnosis. This reminds one of Eliot Slater's work on patients given the diagnosis of hysteria in the 1950s and followed up nine years later (Slater, 1965). He found that of the 99 patients he could follow, only 19 were symptom free. There had been a missed organic diagnosis in a third. Such organic diagnoses as disseminated sclerosis, neoplasms in the central nervous system, vascular disease, epilepsy, dementia, cord compression, and trigeminal neuralgia were overlooked. There were also missed psychiatric diagnoses of obsessional neurosis, schizophrenia, and bipolar affective disorder. Only seven patients at follow-up could be said to have had a true conversion syndrome.

DR HIGGO (*registrar*): Slater's work on hysteria related to work at the National Hospital in Queen's Square (a neurological unit) and might therefore not be typical. Lewis (1975) showed that the majority of patients with hysteria were completely well on follow-up and thus did not have serious organic disease which had not been diagnosed. Some patients still had symptoms closely related to their original presentation. Reed (1975) showed that a majority of patients had genuine psychiatric disorders, or could be called histrionic personalities.

Overall I would suggest that 'hysteria' frequently represents significant psychiatric morbidity. It is incorrect to suggest that 'hysterics' merely have undiagnosed physical illness. Perhaps we should rather see them in terms of abnormal illness behaviour.

DR POOLE: This lady's history is marked by a pattern of grief and loss. It would appear that she uses mechanisms of manic denial, and the mixed affective picture might be understood in this context. You do not necessarily need to invoke the diagnosis of hysterical conversion to accept that these movements may be resolving many different questions for this lady, and thus may be exacerbated and sustained by the mechanism of secondary gain.

DR UPADHYAYA (*lecturer in psychiatry*): I feel that a lesion of the left basal ganglia is the most likely differential diagnosis for the athetosis. It may be that the CT scan did not pick this up. Further brain imaging such single-photon emission tomograms or magnetic resonance imaging could reveal abnormalities in the basal ganglia. These are sometimes very difficult to find. A brief report by Besson *et al* (1988) showed a lesion only on studies of cerebral perfusion in the striatal area. They suggested that such abnormalities indicate a favourable response to drug treatment for torticollis.

PROF. COPELAND (*head of department of psychiatry*): From what you have told us there does not seem to me to be any real evidence that the patient had an hysterical illness in the past. All her symptoms in 1977 seem to be consistent with a mixed affective state, so I would tend to dismiss that diagnosis.

Is this tardive dyskinesia? She has several risk factors: age, female sex, and antipsychotic medication. Kane (unpublished) claimed that affective disorder in schizophrenic patients carried an increased risk. However, as Dr Abou-Saleh pointed out, the picture is atypical in being unilateral and confined to the arm, although, rarely, this can happen. The danger here is to assume that the neuroleptics have brought about the condition, and to overlook a neurological cause.

One is looking for disorders which cause these symptoms, either alone or in combination with psychiatric symptoms. Some we have mentioned, but there are others which are rare. I do not know of any presentations of Wilson's disease or Huntington's chorea which resemble this patient's illness. You will need to persevere with investigations, but often no cause is found.

Regarding treatment, I do not have much to add. If you conclude that this is tardive dyskinesia, there have been several reports of the value of calcium channel blockers (Ross *et al*, 1987; Leys *et al*, 1988), but I do not have any experience of using them myself. I think that tardive dyskinesia is not the diagnosis.

Conclusion

Several abnormal investigations were returned after the case conference. These included a heat inactivation test and positive DNA autoantibody tests. These tests were reviewed and repeated by a consultant rheumatologist. Taking the clinical history as a whole, the complaint of alopecia, and reduced tear production on examination, he was able to conclude that this patient had systemic lupus erythematosus (SLE). This has important implications. The abnormal arm movements might then be seen in the context of discrete cerebral microinfarcts, undetected by CT. (We await the results of nuclear magnetic resonance imaging.)

The excess incidence of neuropsychiatric illness in patients with SLE is well documented and may reach 60% of SLE sufferers. Such neuropsychiatric manifestations can mimic the clinical pictures of hysteria, schizophrenia, and bipolar affective disorders (Feinglass *et al*, 1976). The diagnosis of SLE with involvement of the central nervous system might well provide a complete explanation for the differing psychiatric presentations in this patient and the abnormal arm movements.

A number of drugs are capable of producing serological and clinical features of SLE. These drug-induced lupus syndromes can be caused by anticonvulsants (phenytoin, ethosuximide), anti-arrhythmics (procainamide), antihypertensives (methyldopa), and antibiotics (penicillin, sulphonamides). Chlorpromazine, which this patient received for five years, is also included (Weinstein, 1980). However, on the basis of the repeat tests he had performed, the consultant rheumatologist confirmed the diagnosis of SLE.

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British Journal of Psychiatry (1989), **155**, 712–719

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Contents: Fractured femurs in the mentally handicapped/US visas and 'insanity'/Doll phobia revisited/ Historical melancholia/ECT in old age/Pimozide in pathological jealousy/Syphilis screening/Lipopigment in the CNS/Tardive dystonia/Nicotine and dementia/Depression-dependent exacerbation of TD/Physical morbidity of psychiatric patients/ Benzodiazepines unabashed/Remission of psychotic symptoms after burn injury.

Fractured femurs in the mentally handicapped

SIR: Findings from the studies of Lau *et al* (1988) and Cooper *et al* (1988), on physical activity and calcium intake in fractures of the proximal femur in Hong Kong and in Britain, point to the fact that in order to protect against hip fractures it is important for elderly people to maintain daily physical activities and the required calcium intake.

We have completed a survey of the mentally handicapped population over 40 years of age in four hospitals in Bristol. There were 366 men and 365 women, of whom 55 men and 62 women sustained one or more fractures (72 and 110 fractures respectively). In the survey there were 36 fractures of the proximal femur (16 in men and 20 in women). Most of the patients with hip fractures were severely mentally handicapped and ages ranged from 44 to 77 years (mean age 57.3) in men and from 40 to 73 years (mean age 59.9) in women.

Apart from decreasing physical activity because of severe mental handicap and ageing processes, there were other factors which were impairing daily physical activities and mobility. Nine patients were on anticonvulsant therapy, eight were receiving antipsychotic drugs, two suffered from blindness, and eleven had debilitating physical disorders. The findings illustrate that decreased physical activity and mobility in the mentally handicapped is one of the risk factors for hip fractures in elderly patients.

It is therefore important that, with the marked increase in longevity of the mentally handicapped population (Carter & Jancar, 1983), patients should continue with daily activities as long as possible, regular exercise should be encouraged, and calcium levels monitored, thus helping with protection against hip and other fractures.

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US visas and 'insanity'

SIR: There seems to be a widespread belief that compulsory admission under the provisions of the Mental Health Act 1983 adversely affects a person's ability to obtain a visa to enter the United States of America. We asked 16 mental health professionals (11 section-12 approved psychiatrists and 5 approved social workers) from two local hospitals how they thought mental illness and/or compulsory admission affected the ability of an individual to obtain a US visa: ten believed compulsory admission was the major factor, five were unsure, and one (a social worker) believed it was dependent upon the type of mental illness. Eight professionals said they would be less likely to detain a patient who wanted to obtain a US visa. We know of several recent cases in which the visa issue was considered important in deciding whether or not to detain the patient in hospital.

In order to clarify the situation, we wrote to the Visa Branch of the US Embassy who provided the following information: the US Immigration and Nationality Act stipulates that persons who are or have been 'insane' are ineligible for visas. However, the Attorney General can waive these ineligibilities and a person with a history of 'insanity' who is certified by a competent medical authority to be currently well may be granted a visa (visitor, temporary, or immigrant). Compulsory admission to mental hospital would serve as evidence of an attack of 'insanity' but the effect of such an admission would depend on the patient's recovery.

Thus, contrary to popular psychiatric belief, it appears that compulsory admission may, if it produces a more rapid recovery, actually *help* a patient to obtain a US visa.

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Doll phobia revisited

Sir: It was very interesting to read Hatcher's description of successful exposure treatment of a doll phobia in a 14-year-old boy (*Journal*, August 1989, **155**, 255–257). He notes the rarity of doll phobia despite the ubiquity of dolls in most cultures. Such discordance between frequency of contact with stimuli and fear of them may be partly explained by a prepotency and preparedness of certain cues to arouse fear more than others do in a species as a result of its evolutionary history. Incidentally, the credit for the first description of doll phobia probably goes to Rangell (1952), cited by Marks (1987, p. 396).

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Historical melancholia

Sir: Berrios's (1988) conceptual history of melancholia and depression, while scholarly and deep, is, I would suggest, in parts overstated. He says, for example, that the concept of bipolar disease required a series of conditions that were only met after 1950. Certainly earlier physicians spoke at the least of the continuity of melancholia and mania, for example Boerhaave (1728), Morgagni (1761), and Esquirol (1812) (see Frosch, 1987). Furthermore, it appears clear that the notion of alternating disturbed states of slow, exerted behaviour with fast, even frantic, behaviour can be seen to have entered the popular imagination. Caldwell (1972) has drawn our attention to the fact that the final movement of the sixth of the Opus 18 quartets (written in 1799) was entitled by Beethoven "La Malinconia". The movement consists of six alternating slow and fast sections, the slow sections inhibited, unelaborated, the fast sections bristling with energy, leaps and trill-like figures. That Beethoven recognised what he was portraying is confirmed in a later letter to a friend about another piece contemporaneous with "La Malinconia": "everyone at that time sensed . . . the mental state of melancholia and its phases". That this notion was not new in 1800 can also be seen in Pondourus's description (fourth century AD) that mania is "an intermittent disease which proceeds through a periodical variant . . . it repeats itself once a year or more often . . . melancholia occurs in autumn, whereas mania in summer" (source of quote unlocated).

Good, careful observation is not a recent invention. While theory can determine what we are aware of seeing, through the millennia family and friends of individuals with manic–depressive disease must have been aware of its alternation, its circularity, aware of each phase's characteristic thought contents, feeling states, and activity patterns, aware of the continuity between the phases. The shamans and physicians involved in their care must also have known these facts. We should not delude ourselves that our unassisted senses and reasoning powers are better than those of our ancestors. Changing social structure and new data, real or imagined, lead to newly organised observations and to new explanations, to new theories. Berrios's paper properly directs us to this level of historical inquiry.

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ECT in old age

Sir: We read with interest the paper by Benbow on electroconvulsive therapy (ECT) for depressive illness in old age (*Journal*, August 1989, **155**, 147–152). We also studied the use of ECT in elderly depressive patients (Malcolm & Peet, 1989), but reached somewhat different conclusions.

Evidence is far from conclusive that ECT is the most effective form of treatment for elderly depressed patients. There are few, if any, methodologically satisfactory controlled trials of ECT conducted specifically in elderly populations. Available data from open, uncontrolled trials reveal widely varying response rates, with short-term response rates being much more favourable than long-term rates. This is in keeping with controlled trials in younger patients, showing ECT to have short-term efficacy only (Johnstone *et al*, 1980; Brandon *et al*, 1984). Depression is a chronic disorder, with prolonged morbidity in the elderly, as Benbow rightly points out. The short-term nature of the ECT response necessitates continuation treatment with antidepressants after ECT to prevent relapse. If the clinician recommends ECT and fails to seek an initial effective antidepressant, there is no way of knowing which drug will be effective after ECT.

Furthermore, trials comparing ECT with antidepressant drugs also suffer from methodological defects (Rifkin, 1988) and do not take into account advances in psychopharmacology, such as the use of combined antidepressants and neuroleptics in delusional depression.

With regard to safety, ECT is held to be superior when compared with older antidepressants. However, as Benbow indicates, the cardiovascular side-effects of ECT are not uncommon. Trials comparing the relative safety of ECT and the newer antidepressants, known to be considerably less cardiotoxic than the older antidepressants, have yet to be done.

Finally, end-point states of depression requiring ECT are not reached suddenly. The duration of depressive symptoms may be especially long in the elderly, and in under-resourced services it is often only those who have deteriorated into severe depressive states who are admitted for treatment, by which time ECT may be considered inevitable. A comprehensive community-based service, which can mobilise pharmacological, psychological, and social help at an early stage of the depressive disorder, may well reduce the need for ECT.

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Pimozide in pathological jealousy

SIR: Byrne & Yatham (*Journal*, August 1989, **155**, 249–251) claim that treatment with pimozide was successful but produce no evidence. They are aware that pathological jealousy can occur in relation to alcoholism and one would assume that following admission to hospital this patient would have ceased to drink. In that case one would have expected the symptoms to have subsided in the ensuing few weeks without the use of any drugs; indeed the correct treatment of such a patient after admission would be *not* to give any drugs for some weeks and to review the diagnosis after that time if symptoms persisted. If persisting symptoms then subsided following the administration of a drug, that would be reasonably convincing evidence of the drug's effectiveness; the case report does not state that the patient was managed in this way.

I am bound to comment on the authors' statement that it is "well established" that pimozide is "very effective" in the treatment of monosymptomatic hypochondriacal delusional psychosis. I have tried the drug in a number of patients but found it singularly ineffective. Others have told me that they have had similar experience. It is possible that it has some effect but it is far from "well established" that it is "very effective". On the other hand it *is* well established that morbid jealousy in alcoholics frequently subsides when they stop drinking.

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Syphilis screening

SIR: Boodhoo (*Journal*, August 1989, **155**, 259–262) poses a number of questions relating to syphilis screening in a psychogeriatric population.

Although syphilis remains a cause of reversible psychiatric illness, appropriate studies in patients over the age of 65 are lacking. Nevertheless, as syphilis may remain latent for over 30 years, syphilis serology should be checked at any age and positive results further investigated by examination of the cerebrospinal fluid (CSF) (Weatherall *et al*, 1985). Negative CSF serology excludes active neurosyphilis, whereas a positive result should lead to treatment and follow-up CSF examination (Adams & Victor, 1985).

Until a study in this age group finds evidence to the contrary, we believe that syphilis screening remains an essential investigation.

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Lipopigment in the CNS

Sir: Dowson (*Journal*, July 1989, **155**, 1–11) highlights the uncertainty surrounding the origin and significance of lipopigment in the central nervous system (CNS). Most authors would share the view that lipofuscin is not itself a causal factor in ageing, but rather a by-product, indicating that destructive oxidative processes have taken place (Sohal & Wolfe, 1986). Lipopigment itself may originate from several possible sources, but there is strong evidence to suggest that free-radical damage is an important factor. Damage to biological molecules produces malonaldehyde and other substances, inducing polymerisation of amine-containing molecules. The conjugated Schiff bases thus formed have similar emission spectra to those of chloroform extracts of purified lipofuscin, suggesting a common biochemical link (Tappel, 1975).

Dowson also suggests that chronic neuroleptic administration may protect against ageing, extrapolating from the effects of chlorpromazine on intracellular pigment in rat neurons. It has been suggested that phenothiazines, being heterocyclic compounds incorporating ring nitrogen and sulphur atoms, may act as free-radical scavengers. However, the 'cross-over effect' has also been noted, for instance with promethazine, which may be protective towards membranes at one concentration but deleterious at another (Slater, 1972). There is, indeed, growing evidence to suggest that neuroleptics may themselves induce free-radical damage in the CNS. This has been proposed as one mechanism by which tardive dyskinesia may be produced. Metabolites of phenothiazines, particularly the ortho-dihydroxylated derivatives, have been shown *in vitro* to generate toxic free-radical species (Heikkila & Cohen, 1975). Pall *et al* (1987) demonstrated increased products of free-radical damage in the cerebrospinal fluid of patients taking phenothiazines. In a trial of the antioxidant alpha-tocopherol, a marked reduction in the symptoms of tardive dyskinesia was described (Lohr *et al*, 1988).

The situation is clearly highly complex, as psychotropic drugs and their metabolites may exhibit different properties at various sites. Despite the difficulties of studying esoteric biochemical reactions in the CNS, the results may have considerable therapeutic implications. This line of inquiry therefore merits further research.

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Tardive dystonia

Sir: Cooper *et al* (*Journal*, July 1989, **155**, 113–115) reported tardive dystonia in a schizophrenic patient in his 20s which was worsened by anticholinergic drug treatment. This case is atypical. In a report by Kang *et al* (1986), 57% of patients with tardive dystonia were improved with anticholinergic drugs. Of the other patients with tardive dystonia reported in the literature, there is no mention of exacerbation by anticholinergic agents.

The phenomenon of "delayed-onset dystonia" has been reported by Burke *et al* (1980): eight cases of persistent dystonia appeared years after non-progressive cerebral insults, including perinatal anoxia, trauma, and cerebral infarction. There was no history of neuroleptic treatment. It is interesting to note that the patient reported by Cooper *et al* had a history of prematurity, two perinatal anoxic episodes, epilepsy, and a focus of left temporal spike waves on the EEG.

The brain damage may have acted as a predisposing factor for the development of tardive dystonia in this patient. Another possibility is the occurrence of delayed-onset dystonia in a patient on neuroleptic treatment. One of the diagnostic criteria for tardive dystonia is exclusion of secondary causes of dystonia (Burke *et al*, 1982). Delayed-onset dystonia is one which may easily have been overlooked.

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Nicotine and dementia

SIR: The results reported by Sahakian *et al* (*Journal*, June 1989, **154**, 797–800) on the effects of nicotine in patients with dementia of the Alzheimer type are interesting and clearly warrant further evaluation. We would however like to raise some methodological concerns.

Firstly, the inclusion of cigarette smokers is questionable. There is evidence that prolonged or repeated exposure to nicotine can cause a desensitisation blockade of the receptors (Wonnacott, 1987) and that, as a result, subjects who smoke regularly may be less sensitive to the effects of subcutaneous nicotine. In addition, the density of nicotinic receptors in the brain has been shown to be increased in brain tissue taken from habitual smokers (Benwell *et al*, 1988). Although the possible psychopharmacological consequences of the change in receptor density remains to be established, it seems reasonable to suggest that patients who are also regular smokers may not respond to systemic nicotine in the same way or to the same degree as non-smokers. Therefore, the apparent lack of response to the drug in some of the tests (e.g. the short-term memory test) may simply reflect the heterogeneity of the patient population used.

Secondly, there is wide intrasubject variability in performance on cognitive tests in demented patients. Since the effects of subcutaneous nicotine are of rapid onset it is feasible to test the patients before and after administration of drug or placebo at each session. Positive results with this experimental design would be of greater significance.

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Depression-dependent exacerbation of TD

SIR: I read with interest the case "Depression-dependent exacerbation of tardive dyskinesia" reported by Sachdev (*Journal*, August 1989, **155**, 253–255). The case is presented well, but I would like to draw readers' attention to previous literature on this topic.

Yassa *et al* (1983), investigating patients with affective disorder, found a prevalence of tardive dyskinesia (TD) of 41%, with affected patients being older than those without TD. Yassa *et al* (1987) went on to investigate patients being started on antidepressants. Of 50 patients, three developed TD, two improving on withdrawal of the drugs. They quote a number of authors who have reported both the presence of TD in patients on antidepressants (15 cases) and others describing affective disorder as an exacerbating risk factor for TD in other disorders.

I would support Sachdev in the assertion that current biochemical theories are contradicted by these cases and that new explanations will have to be found. I would add that the model would have to take account of possible predisposing factors (age, sex, previous neuroleptic use, organic damage, alcohol use) as well as concurrent medication and mental state.

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Physical morbidity of psychiatric patients

SIR: I was a little troubled by the study of Honig *et al* (*Journal*, July 1989, **155**, 58–64) looking at the physical morbidity of psychiatric patients. A recent and well conducted study by Ziber *et al* (1989) suggests that, considering all classes of psychiatric patients, the standardised mortality ratio was 2.3. The major causes of death were related to dysfunction of the cardiovascular and respiratory systems, probably because of excessive smoking. Another recent study, by Casadebaig & Quemeda (1989), on mortality among psychiatric in-patients, also commented upon an excess of deaths through cardiovascular and respiratory disease.

The age of patients in the study by Honig *et al* was only 45 years, and hence slightly below the age of major risk for such complications. It is however very narrow-sighted of them not to comment upon the likely illnesses which face the slightly older group of psychiatric patients and not to emphasise the important health education role of the psychiatrist.

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Benzodiazepines unabashed

SIR: It was refreshing to read Kräupl Taylor's article on benzodiazepines (*Journal*, May 1989, **154**, 697–704), following the bashing this particular group of drugs has been subjected to recently. I have used various benzodiazepines to treat anxiety states in the past few years and find them extremely useful. As with any other drugs there should be indications to use them and they can be abused by way of over-prescribing both by doctors and by the public. Whatever the research workers might say, in my opinion, there is a minority of patients who seem to benefit from them even on long-term therapy (more so on a *pro re nata* basis), and I do not think this is due to psychological dependence alone.

I was most surprised to hear about the recent proclamation issued by the Royal College of Psychiatrists pertaining to the duration of benzodiazepine therapy. I think this is an insult to the clinical judgement of doctors, and furthermore could cause confusion among the public. We all can have strong opinions about various aspects of drug therapy, but we should not necessarily impose these on others. (I am reminded of a clinical director who sent out a circular to all the staff members and residents prohibiting the use of intramuscular diazepam, and of another instance where a decision was made to ban the use of triazolam in a leading psychiatric department in Canada.)

In the light of these developments it is also interesting to note the course taken by some of the leading research workers. In the initial phase they bring out numerous research papers describing the virtues of the drug, in the middle phase they are busy publishing papers on the side-effects of the drugs, and lastly they bombard us with research work pertaining to the withdrawal effects of the drugs, and go a step further in condemning some doctors for being overzealous in prescribing these drugs. Most of us are aware of this scenario and tend to take all kinds of psychiatric research and especially 'new and dramatic developments in psychiatric research' with a pinch of salt.

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Remission of psychotic symptoms after burn injury

SIR: Self-incineration is a rare but dramatic way to attempt suicide. Its symbolism as a form of political protest (Crosby *et al*, 1977), or religious phenomenon (Topp, 1973), its relationship to underlying psychiatric disorders (Jacobson *et al*, 1986), and psychoanalytic accounts of its significance (Friedman *et al*, 1972), have all been examined, but very little has been written about the effect of deliberate or accidental burning upon the mental state of the psychiatric patient. We report two cases where psychotic symptoms appear to remit after significant burn injury.

Case Report A: A 31-year-old Afro-Caribbean man was admitted urgently after being found wandering in a mute and inaccessible state. He had been first admitted ten years previously, when hebephrenic schizophrenia was diagnosed, and there had been two subsequent admissions, each characterised by flattened, occasionally fatuous affect, auditory hallucinations, and paranoid delusions. His one full sibling was similarly afflicted, but neither parent and none of six half-siblings had any psychiatric history. His response to treatment with oral and depot antipsychotics had previously been slow, but eventually complete, although he had been lost to follow-up for five years. Informants gave a history of six months of increasingly bizarre behaviour, and when he began speaking a few days later, mental state examination revealed auditory hallucinations and paranoid delusions. Two weeks after admission he sustained 5% mixed thickness burns to his torso after accidentally igniting his bedding while smoking. After initial analgesia and dressing he was transferred to a regional burns unit for skin grafting. He remained free of psychotic symptoms throughout his one-month stay there, and for a further two weeks after his return to the ward, when the earlier symptoms re-emerged, associated with some manic features, and required in-patient treatment for a further six months.

Case Report B: A 67-year-old Caucasian woman with no family history of psychiatric illness was first admitted with psychotic symptoms in 1977. The initial diagnosis of manic–depressive psychosis was revised to schizophrenia in 1984, after several more admissions, with good recovery between episodes. In September 1987 she sustained several fractures in falling from a first-floor window at the psychiatric after-care hostel where she lived. She may have been psychotic at the time, although this is not clearly documented. She exhibited no psychotic symptoms on the orthopaedic ward, and after four months was transferred to a psychiatric hospital pending discharge back to her hostel. After a week she reported auditory hallucinations and exhibited bizarre catatonic posturing. She went missing and was later found lying against a radiator having sustained 5% third-degree burns to her buttock and arm. She was transferred to the general hospital for treatment, including surgery, and for seven months there exhibited no psychotic symptoms, despite withdrawal of her regular antipsychotic medication, until eventually she became deluded and aggressive and was returned to the psychiatric hospital for a further five-month stay.

Physical assault has been suggested as an important treatment for mental disorders in ancient Indian medical texts. The reasons for such an improvement may be similar to those postulated for the repeated self-harm exhibited by habitual self-mutilators, i.e. increased plasma metenkephalins (Coid *et al*, 1983). Increased levels of prostaglandins and/or opioids, whether endogenous or prescribed as analgesics, may account for the apparent effect of burns upon the mental state. We are currently compiling a list of such patients who may then be studied more thoroughly, and would welcome details of similar patients from our colleagues.

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A HUNDRED YEARS AGO

Wandering Lunatics

As reported in the *Daily News* of May 18th, the case of a wandering lunatic was brought before Mr. Haden Corser, the magistrate at Dalston Police-court, on the previous day. The magistrate took exception to the police order on this subject conveying the instruction "that all wandering lunatics are to be taken before a police magistrate and charged"; and he said they should go first to the workhouse and be examined by the doctors before coming to the police-court. Inspector McCarthy said the workhouse authorities were not bound to take lunacy cases from the police. The magistrate put the following remarks upon the charge sheet: "It appears to me that the police order as to wandering lunatics is inconvenient. There is a discretion in which persons so wandering could be taken to the workhouse under the Lunacy Amendment Act, 1885, when a person brought before a justice charged with wandering, and the justice has no medical evidence, but must commit for examination to the workhouse. In my opinion their examination ought to be made there in the first instance." It may well be that a magistrate under such circumstances feels that he is somewhat in a fix; for either he ought to constitute himself a judge of the insanity of the individual, and deal with the case in accordance with the conclusion at which he arrives, or else he must remand the alleged lunatic until a medical examination has been made as to the state of his mind, and this is a cumbrous mode of procedure. A magistrate is well advised in refusing to take upon himself the responsibility of a decision in such cases. Mr. Haden Corser thinks the wandering lunatic ought to be taken to the workhouse for examination by the doctor there before he is taken into court. While we agree that a medical examination of the man ought to be made before he is brought into court, we think the medical officer of the police division is the proper person to make the examination at this stage. So long as the case is a police case, the investigation ought to be carried out by the police officials.

This course is not only advisable in itself as a matter of routine, but it would have the further merit of relieving the workhouse official of the invidious duty of having to certify to the insanity of an individual who, upon that certificate, would very likely be relegated to his care as a lunatic. The confinement of a lunatic in the workhouse at which the certificate of insanity was granted would scarcely fail to set up a feeling of irritation and of antagonism against the authorities there, which would be avoided if the primary certificate were to be signed by the police medical officer of the district.

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Special Review

The History of the National Health Service

In the current furore over fundamental changes proposed for the NHS, it would be much better if everyone involved clearly understood how and why the service was established, how it evolved early on, and what had existed before. A fairly safe bet, though, is that given an MCQ on those subjects, most participants in today's events would emerge with little credit. Yet the whole story is now accessible to them – told by Charles Webster (1988) with outstanding scholarship and clarity, lightened by a slightly acerbic wit.

One surprising conclusion might be that we owe the existence of the NHS not so much to Aneurin Bevan as to Hitler. When emergency planning finally became serious in the late 1930s, enormous numbers of casualties were expected from air attack, so that hospitals were needed to cope with these, but looking at the services available nationally, medical planners found them inadequate and disorganised. Hence the Emergency Medical Service which, says Webster, "plunged the nation into an experiment in integrated hospital planning. Once this step was taken it was impossible to revert to the pre-war situation.... Especially [after] the decision to integrate the mental sector ... the scale of the hospital side ... dwarfed everything else." As Tinker (1989) points out, "owing to their importance as social institutions, hospitals have always been pawns in the political game".

In this, as in so many things, there had been a missed opportunity after World War I, when a primary/secondary distinction in health care first emerged officially, in the Dawson Report. Economic slump in 1921, though, ended any chance that health services might then be substantially reorganised or made more widely available; each separate interest – voluntary hospitals, local health authorities, GPs (mainly depending on private fees), Friendly Societies, the Board of Control – fought its own corner as if the others hardly existed. Though the operation of the Inverse Care Law (Tudor-Hart, 1971) meant that services were most available where they were least needed, there was practically no agreement as to what to do next.

Accelerated by Beveridge's breath-taking assumption that there would *have* to be comprehensive health care, serious planning for it actually began in 1943, at first based on a recommendation that the whole service should be run by about 60 local health authorities. Steering a skilful path through the labyrinth of successive drafts, negotiations, and compromises that went on up to the very eve of the NHS' inauguration, Webster exonerates the Board of Control for at first resisting the inclusion of mental and mental deficiency hospitals. Their argument was that the mental health services could not be reorganised without big changes in the law, which in turn would not be possible without a Royal Commission. This opposition was dropped, however, on the understanding that each of the new health authorities would have a strong Mental Health Committee, and that the Board would keep its own identity, though within the Ministry of Health. When Bevan took charge of the negotiations, he quickly grasped both that unreorganised local government was incapable of running the new service and that municipal control was its most unattractive aspect for medical specialists. Against all expert advice, he decided to nationalise the entire hospital system – a bold stroke which came off triumphantly, though the price was to leave GPs and local health authorities substantially continuing to run their own sectors as before. Webster suggests that Bevan, "thereby sacrificed an opportunity to unify health administration, which had been one of the major themes of early plans for a comprehensive health service". That is true enough, but Bevan may well have been right not to attempt too much at once: taking on the hospitals was in itself a huge new task for the central government departments, since this had been left almost wholly to local authorities or the voluntary sector up to then. But he would probably have been surprised that it took almost another 25 years to integrate community health services with the hospitals. Like many aspects of the NHS, though, the tripartite structure worked better for acute care than for the more chronic disorders, amongst which mental illness and handicap were prominent. This has been a continuing theme ever since, and Griffiths is the latest attempt to provide it with a definitive answer.

What was most surprising, perhaps, was that once the Appointed Day had come and gone in 1948, the furious disputes which had raged up to that point seemed to melt away, all parties recognising that this was the best deal they could get. Almost instantly, it seemed, the NHS had become as much a part of the British way of life as the weather or the monarchy – to be complained about at times, but never seriously questioned. Webster describes this as a "spurious consensus", but considering, for instance, that the most vigorous defence of the existing NHS is being mounted by the medical profession, it is not easy to see in what way it was spurious. Furthermore, whatever political arguments may have gone on around the passage of the NHS Act, the change from a Labour to a Conservative government in 1951 made no significant difference to the way the service was run. From the beginning, the only change wanted by people in general was to have more of the same, it being, as Webster says, "such an improvement over its antecedents that public satisfaction was guaranteed". The NHS involved what he describes as an "ambitious experiment" of aiming to allow the level of care supplied to rise to that of demand, but since demand is potentially infinite, the limitation of that care had to come from the amount of public expenditure allocated to health; and there's the rub, since as much as the general philosophy of the NHS has been generally non-controversial, so its financial limits have continued to be highly problematic.

In one of the most outstanding sections of his book, Dr Webster shows how this whole issue originated in the wildly overoptimistic estimates, both for revenue and capital, that were prepared by civil servants and endorsed by ministers before the service began. In the debates on the NHS Bill, finance was not even raised as a major problem, and it has never proved possible since then to break out of that trap of unreal budgeting. Yet, he says, "there was no excuse for innocence", since both the pre-war and wartime hospital surveys (Godber, 1988) had revealed a "ramshackle and largely bankrupt edifice". If this was to be converted into a "rational, modern and humane hospital structure to serve the whole population" – and that was the clearly stated objective of the NHS – it would be "inconceivable without revolutionary reorganisation and a secular increase in capital and revenue expenditure", picking up the bill "for decades of resource starvation". In fact, almost from the beginning, there was virtual panic in Whitehall and among members of the Government about the revenue cost of the service – an "impression of overspending [which] derived primarily from artificially low expectations"; Bevan's Cabinet colleagues, with whom he was soon at loggerheads on this point, were "conditioned by standards prevalent during the depression". Yet in the five-year period 1949–54, the total increase in annual spending, allowing for inflation (then very low), was actually less than 10%, and most of this occurred in the first two years, when there were considerable start-up problems. In spite of these restrictions, services were modestly expanded, but the downside was that virtually no new hospital building occurred, and even repair of the many crumbling structures was often impossible, while such overwhelming problems as redressing the imbalance of health-care resources between the north and south of the country could not even be considered.

In a process which should be meaningful to psychiatrists, this yawning gap between unreal estimates on the one hand and current expenditures that seemed to be constantly rising (as they were in nearly every part of the world) on the other, gave rise to a paranoid and facile explanation of 'waste'. Though never substantiated, this myth still persists today, and was a prominent motive behind the most recent proposals for change. It was first investigated in 1956 by the Guillebaud Committee, which, far from finding waste, urged a huge increase in capital outlay; however, when they asked for some regional comparisons of health spending per head of population, they were told by the Ministry that this would be a "futile exercise". They did not attempt, though, to compare NHS costs with those in the other sectors of public expenditure, and there is still no clear explanation why capital spending on health remained so consistently far behind that on education, for instance; but having got into that position, it proved virtually impossible to get out of it (Robinson, 1988). (When the Committee was being set up, the Ministry of Health warned that it could have the paradoxical effect of revealing the extent of unmet needs in fields like mental illness and deficiency – "The Treasury are here playing with fire".) Webster points out that the unreal financial basis on which the NHS operated from the beginning has been a factor causing Britain to fall progressively behind other Western nations, who spend up to twice as much on health, as a proportion of gross national product. The NHS has performed wonders with the resources available to it, but it is now seriously at risk from the effects of chronic financial starvation.

Psychiatrists will be particularly interested in the parts of this history which deal with the mental health services; in fact, one of the boldest aspects of Bevan's hospital plans was their absorption into a national system of the mental and mental deficiency institutions, which had previously been a virtual world of their own. However, one of the best opportunities for promoting integration would have been the combination of mental and general units within single Hospital Management Committees – discouraged though, by the Ministry, on the advice of the Board of Control, with the support of the Guillebaud Committee. The large size of most mental hospitals was one argument in favour of separation, and the role of medical superintendents may well have been another, particularly as tensions developed between some of them and their Group Secretaries, who were no longer in the subordinate position of the previous Clerk & Steward. Apart from severe overcrowding (an argument used in successive Cabinets to try to obtain more capital for hospital building), the biggest problem of the psychiatric sphere at that time was the shortage of trained medical and nursing staff. The new national system of medical appointments was modelled on the voluntary general hospital, so that fitting it into the totally different culture of the mental hospital had to be a long and difficult process; between 1951 and 1956, the number of psychiatric senior registrars actually fell from 117 to only 96 in the whole of England and Wales. Outside a few major centres, specialist training in psychiatry was then almost non-existent, and the quality of most recruits correspondingly bad – Webster rightly points out that "data indicating a rise in specialist numbers are not indicative of an improvement in quality". Though the Spens Committee on medical remuneration had recommended that merit awards might be used as an inducement for consultants to serve in unpopular areas or less prestigious specialties, this policy was, as Webster remarks in a piece of studied understatement, "not emphasised". So far as mental nurses were concerned, the abysmal pay and conditions which had sufficed during the Depression years proved to be completely irrelevant to a period of post-war full employment. Nurses' pay was a constant issue almost from the beginning of the NHS, and it remains the same, more than 40 years later. The problem with it is really the same as that of NHS revenue – that percentage annual increases (which may sometimes be actual decreases in real terms) can never put right a situation of starting from the wrong baseline. That would require a completely fresh start, and the conventions of British public finance make such a radical solution all but impossible.

"The major development priority in the mental sector during the early years of the NHS", says Webster, "was modernisation and extension of existing institutions." Yet in practice, practically nothing happened: it was nearly ten years before any significant building took place, and that was nearly all for mental deficiency, where "Provision of extra beds was regarded as the only means to satisfy the long list of urgent cases awaiting admission". In the case of mental hospitals, the Ministry argued, pressure for expansion could be relieved if the growing population of elderly patients could be accommodated in some other way. That meant 'community care', but once again, hardly anything happened for a long time. In 1961, Richard Titmuss pointed out that in real terms, expenditure on community services for psychiatry and mental handicap was actually less than that a decade earlier. The Treasury, which blocked much expansion of residential care for the elderly by local authorities, blamed the health departments for not finding the money for community care by cutting their existing costs elsewhere. Webster believes that the whole planning initiative tended to be left to hospital authorities, because of the weakness of the other two health sectors – and of course, there was no co-ordinating body for 'health' below the level of government – yet organisations which were essentially set up to run hospitals should not have been expected to take the initiative in developing extramural services. As a result, "a precious opportunity was lost to transfer loyalties and resources into the field of community care". Perhaps once again the real problem was that the scale of finance needed to develop such a new system was simply not made available nationally. It is ironic, in fact, that mental handicap, which was then seen as the category most requiring extra hospital provision, is the one in which a 'community care' policy has now been pursued most extensively.

Even after successive Ministers of Health had warned their Cabinets that the mental and mental deficiency hospitals were on the point of collapse, through lack of capital spending that had still only reached one-third of the pre-war level in real terms, after a decade of the NHS. Even when money was available, it was often underspent because every detail of building had to be approved by the Ministry, and because of the generally very poor quality of Regional Hospital Board technical staff – one of the many unfortunate consequences of the NHS' low-pay policy. However, towards the end of the period covered by this volume, another factor was becoming important: in tuberculosis, new treatment methods had very rapidly changed a situation of severe shortage of hospital beds to one where the in-patient needs were quite small. If such progress could happen almost overnight in chest diseases, why not in mental illness (Godber, 1988)? In the mid-1950s, reports from France of a new class of drugs – the phenothiazines – suggested that perhaps this millenium might indeed be about to arrive. The answer in this case, however, was a good deal more complex, but the available information was enough to convince some key medical figures in the Ministry of Health that it would be wrong to build any new mental hospitals, even though the existing ones required large sums of money to make their continued use acceptable. Just after the period covered by this history, the Report of the Royal Commission was published, endorsing a generally non-institutional policy in mental health; once again, though, the Government was to take a *non possumus* view of the financing of community care services, leaving the responsibility to local authorities.

That will no doubt be an important theme of Dr Webster's next volume, as will Enoch Powell's Hospital Plan (Powell, 1988), which was the first attempt since the NHS began to look at national hospital needs in a comprehensive way. Meanwhile, the origins and first decade of the NHS have been superbly documented in what is undoubtedly a major contribution to British medico-social history.

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British Journal of Psychiatry (1989), **155**, 724–733

Book Reviews

Editor: Sidney Crown

Experience in Mental Health: Community Care and Social Policy. By Kathleen Jones. London: Sage. 1989. 165 pp. £22.50 (hb), £8.95 (pb).

Professor Jones writes about her chosen field of mental health policy with ease and directness. At her retirement, she provides us with a review of a major policy issue of the last 20 years – how to provide mental health services outside institutions. She divides the book of eight short chapters into two parts. The first describes policy developments in four countries: Britain, the USA, Italy, and China. The second part, entitled 'Theory and policy', seeks to be more analytical about mental health service ideologies and models.

It is difficult to capture the complexity of national policy debates in a few pages. The underlying structures of health care need to be described – whether there is insurance cover for all services and the whole population, whether doctors are predominantly in private practice or public service, the separation or mixing of primary and secondary care, etc. For mental health services, differences in conception are important – whether to include neuropsychiatry, mental handicap, alcoholism, or elderly people with dementia. Jones describes historical events in each country, but she does not draw themes together in a comparative framework. Only in a later chapter are some of the statistical data presented. The chapters are vignettes rather than analytic assessments.

The second part of the book uses themes – critiques and alternatives to institutional care, evaluation of services, and models of community-orientated care. Values, and indeed politics, pervade these themes, and often I could not agree with Jones' views. For example, she calls normalisation theory 'fashionable', but does not mention its serious importance over the past ten years to mental health service development advisers, such as the Kings Fund. Several patterns of community mental health services are described, but instead of decentralised neighbourhood provision, Jones recommends a 'centre' serving a population of 100–200 000 people – not far from the 1960s district hospital service model. The most valuable section of the book, for me, is a description of the small study in York that has followed two selected groups of long-stay patients after discharge from hospital. The former patients were found in a variety of residential settings, with met and unmet needs. The study also opens the debate on how to measure quality of life as an outcome of mental health care.

Whom is the book aimed at? Psychiatrists have already had the opportunity to learn Jones' negative views of the Italian mental health reform through papers and correspondence in this *Journal.* Despite its readability, the book lacks the impartiality and academic rigour necessary for me to recommend it as an undergraduate text. A good study of this subject is much needed.

Mark McCarthy, *Senior Lecturer in Community Medicine, University College London*

Costs and Effects of Managing Chronic Psychotic Patients. Edited by D. Schwefel, H. Zollner and P. Potthoff. Berlin: Springer-Verlag. 1988. DM 128.

This volume of 15 papers is one in a series on health systems research edited by K. Davies and W. van Eimeren. The first paper, by Schwefel, is a report of a WHO Planning Meeting held at Mannheim in 1983. This meeting was in response to a perceived increase in the incidence of psychotic diseases, and hence a need to study the health economics of their management. He outlines the aims of the research in this area. The second paper, by Leidl, is a summary of the WHO meeting on cost-effectiveness of managing chronic psychotic patients, held at Munich in 1985. Twelve of the remaining 13 papers are based on those given at this conference. They describe studies in Western Europe and North America.

The book is primarily intended for health economists and those planning research projects or new styles of service. It describes a variety of systems for the care of those with chronic psychotic illness, and attempts to compare and cost these varying systems. The general reader will find the descriptions of service philosophies and styles interesting, but may well get lost in the detail of the economic analysis (as I did). Some of the papers which were originally written in languages other than English are perhaps more difficult because of the translation. All the papers are well referenced, and so provide a useful source for anyone contemplating research in this field. They also illustrate the inherent difficulties in the comparison of different styles of services, and should be seen as a warning to those who think that costing health care is a simple exercise for which reliable and valid measures already exist. Each of the papers describes a separate study, and there is no attempt to make overall comparisons between different countries with their very different styles of service and levels of hospital admissions. I think this book would be a most useful addition to a psychiatric library where it could be dipped into by many and studied more intensively by anyone who was looking for methodological information in preparing a project.

A. C. Brown, *Consultant Senior Lecturer, Department of Mental Health, University of Bristol*

An Introduction to Social Psychiatry. Edited by A. S. Henderson. Oxford: Oxford Medical Publications. 1988. 227 pp.

What is social psychiatry? In this introduction, it is defined as "the relationship between disorders of the mind and the human environment". As the sphere of social psychiatry also embraces such concepts as the effects of "social cohesion, shared values, economic conditions, threat by an enemy and the expectation of survival", the prospects for a comprehensive paperback introduction at first sight appear somewhat daunting.

Nevertheless, the scope of material covered in this book is impressive. The author gives an outline of basic epidemiological tools and methodology, and attempts to review key epidemiological findings in relation to all the major mental disorders. There is an excellent chapter on life events research, and the author also covers the social consequences of mental disorder, social treatments, and methods of evaluating services. There is a wealth of key references and suggestions for further reading, drawing widely from the fields of psychology and sociology as well as the psychiatric literature.

Inevitably, given the complexity of the topics considered, the reader is occasionally frustrated by the superficial analysis. At certain points, the author refers his readers on to other references far too early in the presentation of his material. I would have much preferred an expansion of the sections dealing with methodology, with more attention being paid to common pitfalls in epidemiological research. This might have been more useful than the author's attempts to review the frequently inconclusive epidemiological findings of the whole field of mental disorder.

The final chapter examines the future of social psychiatry. Interestingly, in his search for a greater synthesis with other perspectives in psychiatry, Henderson concludes that insufficient attention has so far been paid to the "properties of the individual", and the extent to which we are the architects of our own environment. He sees social psychiatry moving toward the study of the interaction between the domains of the individual and his or her environment, rather than focusing entirely on the latter.

The term 'social psychiatry' itself may now be redundant, because it "does not accurately reflect how we should think about mental disorders and go about our business". One wonders whether one is reading an introduction to the subject or perhaps its obituary. However, this is a useful book for those seeking a reasonably comprehensive and readable review of a complex field of research, and a candid analysis of its future.

Glynn Harrison, *Consultant Psychiatrist, Academic Department of Psychiatry, University Hospital, Nottingham*

The Challenge of Epidemiology: Issues and Selected Readings. Edited by Carol Buck, Alvaro Llopis, Enrique Najera and Milton Terris. Washington: Pan American Health Organization. 1988. 1017 pp. $30.00.

This is an enormous anthology of epidemiological papers. The book is divided into five sections, the first two of which reflect the historical evolution of the discipline of epidemiology. Two sections address the applications of epidemiology in aetiological and health services studies, and the final discussion section examines future perspectives in epidemiology.

The historical sections are largely devoted to the epidemiology of infectious diseases, and the first notable reference to psychological problems appears in D. D. Reid's paper on 'Sickness and stress in operational flying', first published in 1948. Reid's paper exemplifies the value of complementing clinical studies by epidemiological and statistical work.

Morton Kramer's paper uses illustrations from psychiatric epidemiological studies such as the New Haven and the Hutterite studies in order to emphasise epidemiological principles. Prominent among these are understanding correctly the concepts of incidence and prevalence, and the importance of case definition and standardised case-finding methods. The final psychiatrically orientated paper included in the book is the classic study by Goldberg & Morrison of schizophrenia and social class. More than 25 years after its original publication, this paper remains one of the major pieces of evidence for the 'drift hypothesis' as an explanation of the relationship between schizophrenia and low social class.

Overall, the book is rich in the applications of epidemiology in a wide variety of conditions, but relatively few involve psychiatry as the principal component.

D. P. Forster, *Senior Lecturer in Community Medicine, Division of Community Medicine, University of Newcastle upon Tyne*

Human Organic Memory Disorders. By Andrew R. Mayes. Cambridge: Cambridge University Press. 1988. 300 pp. £30.00 (hb), £10.95 (pb).

This book, part of the series 'Problems in the behavioural sciences', seeks to outline the ways in which brain damage in humans causes memory to break down. The author has been attracted by attempts to construct a taxonomy or "periodic table" of memory disorders. This ambitious approach to memory disturbances in humans requires understanding not only of neuropsychological concepts of memory, but of data derived from observations in clinical neurology, and in the other disciplines basic to understanding the brain. Thus the book is occasionally interspersed with short accounts of synaptic physiology, in MNDA receptors, neuroanatomy, and other disciplines. Here lies one of the major problems in attempting such a holistic approach single-handed; a full understanding of all these aspects of brain function simply cannot be achieved by a single individual. Mayes is at his best when immersed in discussions of neuropsychological concepts.

The book is organised in a novel and stimulating fashion. In the first chapter the underlying mechanisms of memory in healthy individuals and in patients with brain lesions are reviewed, quite simply and without attention to any conflicting detail. For most readers this will be a very valuable introduction to the subject. The author himself recommends that many readers should then turn to the last chapter in which he has attempted an overview of the book's main conclusions, outlining the general view of information processing, and storage that emerges from analysis of elementary memory disorders. The central part of the book is concerned with discussions of short-term memory deficits, semantic memory failures caused by cortical lesions, memory disturbances associated with frontal lobe pathology, the specific clinical details of memory impairment and memory preservation in the organic amnesias, animal data related to human memory problems, and the possibility that memory disturbances may be fundamental to the clinical deficits in Parkinson's disease, schizophrenia and multiple sclerosis. Generally, the book is strongest, as one might expect, in the discussion of short-term memory disorders and in clearly delineating disorders of registration from disorders of recall. Newer ideas on interference, forgetting, and the organisation of memories of various types in the 'memory stores' are also well discussed, and the notion of declarative versus procedural memory, including its relation to episodic and semantic memory and to explicit and implicit memory, is clearly delineated. There is much discussion of the notion of modality-specific memory, and of the role of procedural cues memory, and of the role of procedural cues on recall, including the evidence that some memories are accessible only in relation to the circumstantial cues that accompanied their registration whereas others have a more universal context (so called automatic memory).

Running throughout the book, but not explicit to the reader, is the problem of the relation between the neuroanatomy of clinical memory disorders in patient observations and the neuropsychological concepts. The author clearly assumes a hierarchical organisation of brain function on a Jacksonian model, although Jackson himself is not acknowledged. The concept that the brain is organised in procedural modules, hierarchically arranged and revealed for analysis in patients with lesions of this hierarchical system, has given way in recent years to a concept based on distributive systems. In this concept the hierarchical organisation of the brain is modified to take account of interleashed systems of connectivity between areas of the brain concerned with specific tasks, in the neuropsychological sense, a concept that allows for a far more complex set of interactions and, particularly, takes account of the modality and task-specific organisation of the brain that is revealed in lesion studies in humans in a far more flexible fashion.

Taken as a whole, the book is a valuable and intuitively refreshing account of the memory disorders associated with organic disease of the nervous system. It will repay study and may well reorganise many a clinician's or clinical psychologist's concepts on memory disorders in brain-damaged humans. One suspects that Mayes intends a wide readership, judging by the inclusion of a glossary of terms at the end of the book, and by his choice of references which, while not compendious, provide an effective guide to the main authorities and to strings of thought implicit in recent ideas on memory disorders in humans.

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Epilepsy, Behaviour and Cognitive Function. Edited by MICHAEL R. TRIMBLE and EDWARD H. REYNOLDS. Chichester: John Wiley. 1988. 214 pp. £32.00.

According to the preface, this book was the product of a symposium held in Stratford upon Avon and sponsored by Ciba-Geigy. However, it has more the look of a preplanned and preconceived multi-author textbook for which the symposium was used as a launch, rather than the usual reported symposium proceedings. This is to its credit. The book is made up of 14 chapters by appropriate specialists. These are organised into four sections, and each section concludes with a brief discussion. If a simple distinction can be made between cognition and behaviour, then the former, with 10 chapters, easily predominates. Only two chapters clearly relate to behaviour. There is also an opening chapter providing a historical perspective (by Reynolds) and a chapter on mood disturbance (by M. M. Robertson). The range therefore is not so far short of that of an earlier and more ambitious book from the same editors, *Epilepsy and Psychiatry*, but the contributions here are rather less even. There is an excellent chapter on the methodology of cognitive function assessment by J. Ossetin, a brief and characteristically incisive contribution on the relationship between seizures, EEG discharge, and cognition from C. D. Binnie, and a useful review of focal frontal and temporal seizure phenomenology by P. Fenwick. Sections on the unwanted cognitive effects of anticonvulsant drugs pop up all over the place, most attesting to the superiority of carbamazepine over other competitors. This is not an easy area to research, even less to read about and for those readers who do not have epilepsy clinics, the account provided in Ossetin's chapter may provide a more than adequate summary. There is an excellent section on epilepsy in childhood. This is a book that can be recommended without reserve to those who spend a fair proportion of their professional lives dealing with epileptic patients. Others (and these will include the majority of psychiatrists) should encourage their local library to make copies available.

BRIAN TOONE, *Consultant Psychiatrist,*
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Current Topics in Neuroendocrinology. Edited by D. GANTEN and D. PFAFF. Berlin: Springer Verlag. 1988. 335 pp. DM 175.

This is an excellent review of the neuroendocrinology of depression, written in a form that will be accessible to someone who is developing an interest in biological psychiatry.

The first chapter, by Frixe, describes the genomic and non-genomic actions of oestrogen, glucocorticoids and thyroxine. I found these extremely interesting, and they could well be relevant to puerperal psychosis and the psychoses associated with Cushing's syndrome and myxoedema. There follows a fairly standard chapter on CRF and depression, which includes the hypothesis that CRF overproduction may cause depression. I don't believe this hypothesis, since CRF overproduction seems to be present also in non-depressed patients with agoraphobia and anorexia nervosa, but the argument is interesting and the clinical effects of CRF antagonists will be of great interest.

Mendlewicz & Linkowski give a scholarly and appropriately cautious review of hormonal rhythms in depression. Other highlights include a thorough review of adrenoceptor function in depression by Matussek, Mettzer on 5HT and hormones in depression, Janowsky on acetyl choline and hormones in depression, Post on kindling, Ferrier & Crow on CCK in schizophrenia, and quite a bit else.

I strongly recommend this book.

STUART CHECKLEY, *Consultant Psychiatrist,*
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Can We Prevent Suicide? By DAVID LESTER. New York: AMS Press. 1989. $34.50.

David Lester is a well-known figure in suicide research. During his distinguished career he has published numerous papers on suicide, counselling, and related issues. This short book comprises twelve essays or papers on subjects related to suicide, much of which has been published elsewhere, but none of the papers are direct copies of previous work. It is a fascinating and valuable volume; fascinating because the reader can follow the evolution of the author's views over a period of years and see that it has been profoundly influenced by his acquisition of knowledge about his subject, and valuable because it explores the subject broadly and critically relates suicide to other aspects of the human condition.

It is difficult to pick out any one particular part of the book for special attention. The chapters addressing the question of whether we should prevent suicide are particularly interesting and challenging, and have a relevance that goes beyond suicide and attempted suicide. There are two chapters (or essays) on telephone counselling; these too raise important issues with wider implications than the overall title of the book would suggest. The section on the possibility of suicide prevention starts with a somewhat pessimistic chapter, and ends with a more optimistic view. In his introduction Lester explains that the earlier chapter was written before he had assimilated the data on the effects of gun control laws on the incidence of suicide. His opinion was changed by those data. He says, "The impact of strict handgun control statutes on suicide rates have convinced me that restricting the methods available for suicide will have an impact on the suicide rates". Interestingly, this view is similar to that held by William Farr, who wrote in 1863, "In certain states the mind appears to be fascinated ... by the presence of a fatal instrument ... and the withdrawal of the means of deaths suffices to save the life"!

Lester's new book deserves to be read, studied, and discussed. It is an important contribution to the literature.

R. D. T. FARMER, *Professor of Community Medicine,*
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Life's Preservative Against Self-Killing. By JOHN SYM. Routledge: London. 395 pp. 1989. £29.95.

In the space of seven years, between 1974 and 1981, Ida Macalpine and her son Richard Hunter, the orb and sceptre of British psychiatric historians, vanished from the scene. They left behind them a vast storehouse of knowledge, including a series of reprints of psychiatric monographs. All of them are of prime importance in that they resurrected seminal works which, because of their rarity and costliness, are unavailable to the ordinary reader, or, indeed, to the general run of psychiatric libraries. The book under review follows this honourable tradition, and the scholarship of Michael MacDonald, Professor of History at the University of Michigan, who writes the introduction, compares very favourably with these written by his august forerunners.

John Sym (?1581–1637) was a minister of religion at Leigh in Essex. He was thus an exact contemporary of Robert Burton (1577–1640), who was also in Holy Orders, but whereas Burton's *Anatomy of Melancholy* is perhaps the most famous and most frequently reprinted of antiquarian psychiatric texts, Sym's treatise seems to have dropped out of history.

What Sym's work brings out so well is the unrelenting condemnation of suicide at the time when he lived and wrote. It was considered a species of murder, condemned by the law, by religion, and by folklore. It was a sin, "most hainous and most to be abhored in humane society". It was diabolical. Those posthumously found guilty by a coroner's jury of *felo de se* were savagely punished. They were denied the customary rites of Christian burial, and instead were buried face down at night in a public highway and pinioned with a wooden stake. Their properties and worldly goods were forfeited to the crown.

Sym was a militant puritan, and ostensibly subscribed to the universal abhorence of self-killing. And yet, paradoxically perhaps, he acknowledged that self-destruction was not uniformly determined, but had a variety of causes, including melancholy – that is, mental illness. His long personal experience in giving what help he could to potential suicides had led him to believe that suicide may be prevented "not so much by arguments against the fact ... as the discovery and removal of the motives and the causes" – a singularly enlightened approach and one far in advance of his time. Furthermore, it would appear that he was in practice much more tolerant of self-killing than the majority of his contemporaries, both clerical and secular.

This is a book to be warmly welcomed, not only for its intrinsic scholarship, but because it succeeds in finding room for Sym in the pantheon of early observers of the human condition alongside, for example, Robert Burton and Timothy Bright whose work, incidentally, he complements.

HENRY R. ROLLIN, *Emeritus Consultant, Horton Hospital, Epsom, Surrey*

Problem-Solving Therapy for Depression: Theory, Research and Clinical Guidelines. By ARTHUR M. NEZU, CHRISTINE M. NEZU and MICHAEL G. PERRI. Chichester: John Wiley. 1989. 274 pp. £19.15.

This book provides a valuable addition to the existing literature on the therapy of depression, and discusses a new model of treatment for this important disorder. Divided into two parts, it deals first with the existing behavioural and cognitive models of treatment and asks the pertinent question "Why another theory of depression?" It then proposes the problem-solving model as a multifactorial approach which can link and incorporate key features of other models, outlines its theoretical background, and shows how it can be applied to the treatment of depressive symptomatology. The role of social and life events, biological and genetic factors, previous history and learning experiences, and the problem-solving process itself are used to show how clinical depression may be caused by a variety of factors, and to support the new treatment model put forward. The chapter dealing with the step by step processes of the problem-solving approach is particularly clear and useful.

The second half of the book concentrates on the ways in which problem-solving concepts can be applied to clinical practice, and is well illustrated by examples, including dialogue. A short section on "Pitfalls to avoid" is helpful, even for the more experienced therapist. I particularly liked the clear definitions of terms used throughout the book, and the summaries at the end of each chapter. For example, 'Brainstorming' is a much-used word nowadays, and my understanding of it has been clarified and extended.

All in all, this is a well-presented volume which integrates theory and practice effectively, although it is slightly marred for me by the somewhat tortuous sentence construction. Reasonably priced, it deserves to be read by all those concerned with the care of depressed people.

RHINEDD TOMS, *Consultant Psychiatrist, Severalls Hospital, Colchester*

The Mind Observed: The Mental State Examination. By ASHLEY BUSH. Melbourne: University of Melbourne. 1989. 55 minutes. $\frac{3}{4}$" U-MATIC, $90.00; $\frac{1}{2}$" VHS, $65.00.

The examiner feels a mass in the right hypochondrium, and without needing to cup open the abdomen he can be fairly certain that the mass is a liver. "A similar philosophical mechanism is in operation in the Mental State Examination", begins this videotape. Philosophy apart, what follows is a good lecture delivered at a cracking pace by a personable Australian psychiatrist on the Mental State Examination. However, it is illustrated by a series of doctor/patient interviews which have the sound turned down very low. As the lecturer pauses for breath, one can occasionally make out what is being said, but often it is not relevant to the commentary.

In the last few minutes of the video we can get to hear as well as see the interviews, and titles appear, identifying the phenomena as they flash by. Unfortunately, the effect is often humorous. For instance, a lady says that she feels lonely and a title appears saying THEMES OF LONELINESS. She says she wants counselling, and the title says INSIGHT: GOOD. Sometimes the titles prejudge the issues, as when FLATTENED AFFECT appears after a few seconds of an interview, and sometimes they are hard to follow, e.g. AFFECT UNREACTIVE (NARROW).

The video is of good technical quality, and the acting is very convincing. Features that make it of limited use to British audiences are that the examination is presented in a rather different order than is used in the UK, the distinction between mood and affect appears idiosyncratic, and the classification of thought disorder is old-fashioned.

The content of the lecture would be better presented in a book or a handout than on video. The lecturer, in an attempt to be comprehensive, produces a rapid stream of complicated psychiatric terminology without adequate definition or illustration, and there is no opportunity to stop the video and discuss what has been said. Far better to have the actors more and the lecturer less.

PAUL WOLFSON, *Research Psychiatrist, United Medical and Dental Schools, Guy's and St Thomas's Hospitals, London*

Modern Perspectives in Psychiatry No. 11. Modern Perspectives in Psychosocial Pathology. Edited by JOHN G. HOWELLS. New York: Brunner/Mazel. 1989. 358 pp. $40.00.

This is the 13th volume in a projected 15-volume series which is, in the editor's words, an "international encyclopedia of psychiatry". This volume aims at examining how psychopathology in individuals and families impinges on society and how social psychopathology can arise.

The topics covered are varied, with chapters such as 'Social phobia', which one might expect to find any textbook of psychiatry, and 'Cults and new religious movements', which I have not had the opportunity to read much about. The inclusion of topics which were out of the mainstream of my reading but which were nevertheless interesting was something that I found to be particularly appealing.

The first six chapters focus on children. Topics covered included child abuse, child molesters, incest victims, and volatile substance abuse. These were well written and very accessible, enabling a general adult psychiatrist to easily grasp ideas and approaches to treatment. The middle section is concerned with the psychosocial aspects of particular pathology, and there are chapters on alcohol abuse, pathological gambling, homicide, and agoraphobia. Finally, there are several chapters on the pathology arising within social groups, with titles such as 'Terrorism' and 'Social disaster'. The latter describes the psychopathology occurring as a result of such events as Hiroshima and the Coconut Grove fire.

The editor emphasises the international nature of this series. However, judging from this volume there is a large North American bias; 16 of the 20 chapters are written by authors working in the USA, two are by Australians, and two come from the UK. This is sad, as I feel that certain topics, particularly the chapter on the homeless mentally ill, which was well-written by an American psychiatrist, would have benefited from an international perspective. Also, calling the series an encyclopaedia is slightly misleading. The editor admits in his preface that there is no attempt to fully cover the field in this volume, and this is true.

I enjoyed reading this book, and felt I had learnt something from it. I would not advise individual psychiatrists to buy it without first assuring themselves that a number of the topics would be of interest. It would, however, be a good addition to any psychiatric library.

CHRISTOPHER A. VASSILAS, *Clinical Lecturer in Mental Health, University of Bristol*

The Psyche and Schizophrenia: The Bond Between Affect and Logic. By LUC CIOMPI (translated by D. L. SCHNEIDER). London: Harvard University Press. 1989. 327 pp. £27.95.

This is a profoundly positive book. Ciompi reviews Piaget's theory of cognitive development and links this with psychodynamic theories of affective development. The combination is then linked with recent research on schizophrenia. Ciompi regards schizophrenia as a vulnerability to psychotic breakdown under stress and a risk of progression to chronic invalidism. He recommends treatments which combine positive respect for the patient, pharmacotherapy, and environmental manipulation. He writes with obvious concern and experience and an impressive breadth of knowledge; he acknowledges the lacunae in these theoretical and practical models; and the translation is clear.

In his theoretical synthesis in Chapter 6, 'On schizophrenia', Ciompi respects the dignity and self-determination of the patient while keeping both scientific clarity of thought and compatibility with experimental evidence from genetic, biochemical, and neuroanatomical theories. This contrasts with other theoretical summaries which are so often expressed in a reductive manner difficult to reconcile with self-determination for anyone! That chapter is recommended reading to anyone. The chapter on treatment which follows is weaker, but still useful. I strongly recommend this book to libraries for these chapters alone.

The previous five chapters address the subtitle: *The Bond Between Affect and Logic*. Ciompi suggests that the individual's consciousness is a built on a genetic endowment by alternating affective and cognitive development through Piagettian assimilation and accommodation of the family and social environment. This argument is interesting, but lacks detail on the nature of *Affektlogik* (the title of the 1982 German edition). This lack of a convincing core process is disappointing, and is compounded by prolixity.

Ellis' rational emotive therapy and Ryle's excellent cognitive analytic therapy have already brought together the affective and cognitive. Ciompi goes further with schizophrenia, but he too lacks a real "bond between affect and logic". He is surely right to discuss language, consciousness, self-consciousness, and self-determination, but the whole still lacks something.

This state of affairs is analogous to number theory: with cognitive and behavioural theories we have the rational domain; the addition of psychodynamic theories, like the addition of $\sqrt{2}$ and π, gives a deeper grasp of the neurotically 'irrational'; but without the magical introduction of i, the square root of -1, we still fail to comprehend psychotic *Affektlogik*. Anyone seeking such comprehension should read all of this book with Matte Blanco's works: *The Unconscious as Infinite Sets* (Duckworth, 1975) and *Thinking, Feeling and Being* (Routledge, 1988). These take you much nearer to a bond between affect and logic.

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Treatment of Patients in the Borderline Spectrum. By W. W. MEISSNER. New Jersey: Jason Aronson. 1989. 625 pp.

An increasing amount of technical literature is devoted to the study of the concept of borderline personality patients. This book represents a major addition to that literature.

Meissner is a medically qualified professor of psychoanalysis based in Boston, Mass. He has published widely on the borderline personality since about 1971. He is also a Jesuit. This is very interesting to a Catholic psychiatrist like myself, and I was a little disappointed that he didn't mention what impact this has on his practice. He does say that he is a Jesuit once in the book, and then only fleetingly. I would be interested to know how he dresses during work, and how his clients, of many different persuasions, react to this. His remarks and quotes, when relating to the fantasies of clients, are very explicit. This is all very correct, but it would be interesting to know how he copes with the sexual material so frequently presented by the regressives on the couch or the resistors who sit upright.

Meissner's thesis is that the usual definitions of borderline personality are too restrictive and may account for the strongly negative experiences of therapists. DSM-III-R and other definitions, he would say, are concerned with "lower-order" patients, more primitive in their development, preoedipal and unanalysable, but often perhaps benefiting to some degree from supportive techniques or, less remarkably, from psychoanalytical psychotherapy. They are very prone to regression, often psychotic, and may be helped by medication aimed at target symptoms, such as antidepressants for affective symptoms and neuroleptics for thought disorder.

Meissner recognises major borderline traits in less disturbed and disturbing patients. He stretches the definition to form a spectrum bridging the gap or 'borderline' between psychosis and neurosis. The "higher-order" patients are relatively capable of being psychoanalysed, although they may regress severely for short periods and often respond to being sat up and a period of more active therapist involvement.

The author's abiding message is that the therapist must pay more attention to the therapeutic alliance than to transference issues. He deals lucidly with the therapeutic relationship, the process of therapy, and adjunctive therapies (family therapy, short-term therapy, hospital admission, and drugs). There is an excellent chapter on the different theoretical approaches to borderline patients, e.g. those of Kernberg, Winnicott, Searles, and the followers of Klein.

The material of this book is provocative and illuminating. However, Meissner's practice is selective in that it is American and private. There is a considerable gap in the psychotherapeutic/psychoanalytic literature on how to manage such cases in public practice. Psychoanalysts and large libraries should have a copy of this book.

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An Introduction to Clinical Child Psychology. Edited by STAN LINDSAY and GRAHAM POWELL. Aldershot: Gower. 1989. 341 pp. £35.00.

This book is presumably intended for trainees in clinical psychology, although this is not made explicit in the editors' introduction. From the perspective of a psychiatrist, it has some similarities with the various introductory texts in child psychiatry, but is overall less comprehensive and laid out less systematically, although one or two subjects are treated in much more detail.

The first four chapters are concerned with general issues of investigation and treatment in clinical child psychology, the first two by Yule, and the second two, each headed "practical issues", by the editors. Unfortunately, this division of labour leads to some repetition of similar material. Yule's chapter on investigation would be very helpful to most trainee child psychiatrists. The same cannot be said of his chapter introducing treatment, which is very unbalanced. Behaviour modification is described in considerable detail, while individual psychotherapy and family therapy are dismissed in a few sentences as of dubious value. While behaviour therapy can be seen as an area of special expertise for clinical psychologists, this emphasis fails to acknowledge the considerable numbers of the profession working primarily as family therapists.

Sections on specific topics follow, mainly consisting of single chapters. That on problems in people with mental handicap is a useful overview, and the very detailed one on social behaviour in children and adolescents is particularly helpful. The chapters on problems in adolescence and 'physical problems' (incorporating neuropsychological problems) are more patchy. For example, antisocial behaviour is covered in some detail, school refusal and sexual misbehaviour are treated rather superficially, obesity has a short paragraph, and anorexia nervosa is not mentioned.

One of the most useful features of the book is the extensive bibliography at the end of each chapter. Many of the references will be familiar to child psychiatrists. Apart from the editors, who are (or were) both clinical psychologists at the Institute of Psychiatry, the other contributors are not identified except by surname and initials at the beginning of each chapter. This is irritating for the reader, and seems a discourteous omission.

Although this is an attractively produced hardback book, I do not think the cost is justified by the contents, and would doubt that many trainees would wish to buy a copy.

Patricia Ainsworth, *Lecturer in Child and Adolescent Psychiatry, University of Manchester*

Problems of Pre-School Children. Edited by Naomi Richman and Richard Lansdown. Chichester: John Wiley. 1988. 243 pp. £19.95 (hb), £7.95 (pb).

It takes a certain command of one's subject and confidence in one's ability to communicate it to be able to write and edit a book such as this that discusses the problems of pre-school children clearly, accessibly, and without recourse to jargon. The text is aimed at a wide audience of carers and professionals who work with young children. It makes no assumptions of prior knowledge of children's development or psychology.

The editors emphasise two main themes – firstly that early childhood is a time of adaptation and change, and secondly that all behaviour results from an interaction between the child and the effective social environment. The chapters are written by the editors and close colleagues from the Hospital for Sick Children in Great Ormond Street, and this, together with their careful editing, lends a coherence to the text.

In the first three chapters, Richman looks in turn at the stresses in families that may lead to problems in children, at the myriad of changes in society (such as lack of day care facilities in affluent Britain) that place stress on families, and at recent research on early social relationships. All this is done with great compassion and feeling for the needs of the child in his or her environment. Graham summarises genetic and physical influences on development whose action must be understood even when interventions are environmental.

Lansdown then follows with three chapters overviewing language development, the clumsy child, and learning difficulties. In the latter, he discusses both mental handicap and specific learning difficulties, and it might have been better to separate the two topics. A sensible discussion on child abuse – both physical and sexual – is followed by a superb chapter by Richman in which she provides an overview of behavioural and emotional problems. Douglas then covers behavioural management of common problems in a deceptively clear way, covering many topics and giving good advice that is clearly informed by clinical practice.

Jenkins & Milla provide a good example of how detailed understanding of mechanisms helps clinical practice. They summarise the development of feeding as a prelude to discussing failure to thrive, although the chapter covers all eating disorders. McGuire provides a less satisfactory discussion of gender differences, arguing, unsuccessfully from my point of view, that most are environmentally determined. Feminist perspectives are not necessarily scientific ones. Her chapter on child care away from the family poses interesting challenges to widely held beliefs about day care but, surprisingly, she does not discuss fostering or adoption.

The book finishes with a chapter on the functions and values of play (Richman & Dawe) and on the law as it appears to children (Bieber & Taylor). The latter will be helpful for my clinicians so it is unfortunate that it does not point out the duty placed on NHS professionals by the 1981 Education Act to inform LEAs whenever they suspect that a child may have special educational needs. Working with pre-school children, this must be a common occurrence.

This book admirably attains its objectives. It places the problems of pre-school children in a social context and draws on up-to-date research findings to clarify the mechanisms whereby problems develop. The simple, direct style of writing, with appropriate summary charts and no references in the text, will make it accessible to many carers, and thereby can only improve the wellbeing of pre-school children.

William Yule, *Professor of Applied Child Psychology, University of London, Institute of Psychiatry*

Interprofessional Consultation. By Derek Steinberg. Oxford: Blackwell Scientific. 1989. 134 pp. £15.95.

Steinberg's short, clear and well-written book describes the principles of consultation between professionals, which he distinguishes from consultation with patients, referred to as "clinical consultation". The author is a specialist in adolescent psychiatry, and many of his illustrations are taken from his own experience. However, he is careful to discuss consultation in other settings, and his examples cover a wide range of general and psychiatric hospital community settings. Theory is succinctly summarised, and the book is principally concerned with the practical issues of how to carry out consultation and how to avoid and to deal with problems.

The most important chapters are those that describe the basic principles of consultation and a model for practical work. The former examines when consultation is useful, who should be involved, and what areas of work may be covered. This concludes that "the aim is to help the consultees stand back from the task and, less hampered by over-involvement and tension, to think more clearly and to use to the full his or her imagination and capacity for inventiveness and good management". The chapter describing a model presents a scheme of consultation, beginning with the initial contact and the first consultation and then describing the processes of working together towards review and eventually ending the consultation. Steinberg makes it clear that this consistent and clear model can be adapted to a wide variety of situations, ranging from the briefest of contacts to a prolonged series of meetings.

I started this book with a scepticism induced by well-known authors on the subject who imply an omniscient consultant able to spread enlightenment in a manner that seems to bear little relationship to one's everyday clinical experience. Steinberg's consultation with his reader is more modest, more reassuring, and much more informative. He is sensible, cautious, realistic about problems of multidisciplinary work, and helpful about solutions. He suggests how the consultant can clarify his role and agree what he is attempting to achieve with those who are consulting.

I found this a very helpful book. I also found it easy to read, and I enjoyed Steinberg's cartoon illustrations. I recommend this book.

RICHARD MAYOU, *Clinical Reader in Psychiatry, Oxford University*

The Therapeutic Community Movement: Charisma and Routinization. By NICK MANNING. London: Routledge. 1989. 245 pp. £13.95 (pb), £25.00 (hb).

Interest in therapeutic community ideas has followed something of a sinusoidal path since 1946, when Main introduced the term to psychiatry. After a period of enthusiastic acceptance of the concepts and rapid development of their implementation, psychiatric preoccupations changed and there was a period of relative decline. The recent re-emergence of commitment to what this book correctly identifies as a 'core' of theory and practice which may vary substantially between one local manifestation and another has been accompanied by increasing professionalism and a growth in the research base for therapeutic community work.

This excellent book accomplishes several things. Firstly, it is a social history of the therapeutic community movement – chiefly in Britain, but drawing also on the author's experience in Australia. Manning, now a social scientist at the University of Kent, was research officer at the Henderson Hospital for some years, and is well placed to record this history and to set it within a sociological framework – the progression from a reliance on charismatic leadership to the adoption of the more sober and routine approach of current practice.

Secondly, the book refers to, and sets in context, a fair amount of the empirical research which even in its less popular days the therapeutic community movement continued to generate. Few areas of 'milieu studies' or of the theory of therapeutic organisations have in fact attracted such persistent interest. Thirdly, there is a detailed report of a study by Janine Lees and the author of Richard Fellowship houses in Australia. Using path-analytic statistics, this claims to be a more sophisticated method than any hitherto applied to the evaluation of a residential regime. It demonstrates clearly that in this instance the observed outcomes cannot be accounted for by a combination of spontaneous remission and the careful preselection of 'suitable' patients, but must be contributed to by their experience in the community itself.

In all, this book is strongly recommended to general psychiatrists interested in the structure and management of therapeutic regimes.

D. W. MILLARD, *Fellow of Green College, Oxford*

Sleep and Dreaming. By JACOB EMPSON. London: Faber and Faber. 1989. 258 pp. £12.99.

Many negative book reviews conclude with a statement that the reviewer is uncertain as to which audience the author was aiming the book at. This excellent book on the subject of sleep and dreaming provides a range of information which would be of interest to and accessible to anyone with no specific knowledge about sleep and dreams, and yet manages to include sufficient literary and scientific information so that even seasoned sleep researchers will find interesting nuggets and unusual insights. Perhaps the author has been at an unfair advantage in achieving this unusual accomplishment by having carefully chosen a father who was a Professor of English Literature.

In the introductory chapter Empson elegantly and eruditely covers historical and literary facets related to dreaming, including a brief mention of psychoanalytic dream interpretation. Subsequent chapters deal with measurement of sleep, the experience of sleep and dreaming, sleep quality, and the function of dreaming and sleep separately. The chapters on the psychology of sleep and behaviour of sleep are, not surprisingly from a psychologist, particularly well done, other than the section on exercise and sleep (an area in which I have a 'vested interest' and different view). The section on sleep disorders will be too rudimentary for the professional who may treat sleep disorders, and is definitely more orientated towards the general rather than specialist reader. This section is uneven in its lack of comment, for example, about the dangers associated with night terrors, and gives limited simplistic advice which may lead lay readers to presume that no further help is available for more serious sleep disorders. Separately, Empson does emphasise the dearth of clinical sleep facilities within the UK.

Other positive features in this book were the sense of getting to know the author through the book, the author's use of examples from related disciplines in clarifying complex issues, and the weaving in of aspects of the philosophy of science. The book draws heavily on British literature. The difficulty in locating references (which are reasonably collected at the back of the book for those not wishing to bother with details of journal articles in this easy read, but which could have had chapter titles and top of page headings rather than simply 25 pages of 'Notes') is irritating. The quality of the figures and illustrations is unnecessarily poor, and in some cases the author reports information somewhat uncritically.

Many psychiatrists will enjoy reading this blend of leisure and work-related subject matter.

COLIN M. SHAPIRO, *Senior Lecturer, Department of Psychiatry, University of Edinburgh*

How Does Treatment Help? On the Modes of Therapeutic Action of Psychoanalytic Psychotherapy. By ARNOLD ROTHSTEIN. Madison: International Universities Press. 1989. 232 pp. $32.50.

This densely packed and thought-provoking book is the fourth in the workshop series of the American Psychoanalytic Association. By the time I reached the discussion section I felt I needed to come up for air; it is probably better read in sections rather than one or two sittings.

In general the contributors, struggling in a vital but controversial area, stick to what they know best, their own area of expertise and clinical practice – so much so that at times it is difficult to relate the clinical examples to the underlying theme of the endeavour. Surprisingly, only one contributor mentioned research as making a contribution, and the distillate of Luborsky's views quoted here amounts to the rather likely conclusion that the less sick one is and the more adequate one's functioning prior to therapy, the greater the likelihood of being helped. Not all contributors broke the question down further, although Loewald asks, "Help for the moment or in the long run? Help the patient to run his life better, his relations with others, his work? Help him to understand himself better, and if so how would that help him to be less miserable, to master his conflicts better?" To be sure, many if not all the contributors discuss factors that most therapists would consider important: interpretations, insight, reconstruction, working through, and "corrective emotional experience", although most contributors hasten to dissociate themselves from Alexander & French's original description. There was considerable discussion on the relative importance of insight versus the relational aspects of the transference, eloquently termed by Levenson the "message in the bottle" versus the "laying on of hands".

The most stimulating chapter is Spence's discussion paper using the analogy of the 400-year search for the cause of scurvy to suggest that perhaps in therapy we are still in the position of the helper of of scurvy-prone sailors – many theories and many hypotheses, but in the end, not enough lime juice.

TERESA BLACK, *Specialist Senior Registrar in Psychotherapy, Gaskell House, Swinton Grove, Manchester*

Treating Couples: The Intersystem Model of the Marriage Council of Philadelphia. Edited by GERALD R. WEEKES. New York: Brunner/Mazel. 1989. 352 pp.

Creation and nurture of human life requires couples – heterosexual partners, and then the nursing couple of infant and care giver. So the idea of creative and secure pairing has the utmost emotional importance for everybody, and any professional working with couples who feel destructive and despairing together needs reference texts which offer some reliable containment for her or his anxieties.

Treating Couples goes a considerable way towards providing this. The Philadelphia 'intersystem approach' is a brave shot at combining 'family systems' understanding of three or four family generations with behavioural task-setting, teaching of 'relationship skills', fostering rational understanding of the self and the partner, and modelling respect for feelings. Such an attempt requires a determined and constructive optimism, and this spirit informs the book, which gives a comprehensive survey of the work of the Marriage Council of Philadelphia, and thus includes papers by practitioners on almost every aspect of couple therapy. It demonstrates understanding the couple's problem, structuring the treatment, technique, and termination as practised by the Marriage Council, covers some important clinical issues (spouse abuse and effects of divorce on children, for example), and offers two interesting papers on theory. It is a thorough, lucid, and useful text for anyone who wants to understand and (especially) practice couple therapy. The wilder shores of love remain unvisited, but on a humane and rational eclectic vogage round the treatment of couples, this is perfectly appropriate.

SASHA BROOKES, *Trainee in Marital Psychotherapy, TIMS, London*

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NEGATIVE SYMPTOMS IN SCHIZOPHRENIA

Symposium held at
Charing Cross Hospital
17–18 September 1987

Edited by
Thomas R. E. Barnes

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Introduction

THOMAS R.E. BARNES

The papers in this supplement represent the proceedings of a conference held at Charing Cross Hospital in September 1987. The stimulus to organise this meeting was the difficulty experienced in our department when trying to define and rate negative symptoms for both clinical and research purposes. A central aim of the meeting was to examine the reliability, validity and utility of the available rating scales for negative symptoms. In one of the sessions, videotaped interviews with schizophrenic patients were presented. Using selected scales, negative symptoms were rated by those attending the meeting, who then had the opportunity to discuss their ratings with clinicians familiar with the scales and, in some cases, the authors of the rating instruments.

There are particular problems with the development of rating scales for negative symptoms. Operational definitions are difficult to generate for features that represent a relative absence of function. If they are considered as a loss of normal function then, by definition, severity must be rated on a continuum from normal. This raises the question whether it is possible to determine a criterion level of severity to identify the presence of a 'pathological' symptom. Further, each item will need to cover a wide range of functioning, from normal to virtually complete absence of function. An adequate number of scale points is required to allow for rating on, for example, poverty of speech, from a normal amount of speech through to muteness. Too few scale points will artificially reduce variability while too many may overwhelm the rater.

The current scales for rating negative symptoms each cover a range of items with a core group of symptoms, primarily affective flattening and poverty of speech, common to all. Otherwise, they reveal a variety of interpretations as to which features warrant inclusion as negative symptoms. While the majority of items refer to clinical signs and symptoms, other items reflect psychosocial performance and neuropsychological impairment. The scales discussed in this supplement are the Krawiecka (or Manchester) scale (Hyde, p. 45), the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, p. 49), the negative symptom scale of the Positive and Negative Symptom Scale (PANSS) (Kay *et al*, p. 59), the Psychological Impairments Rating Schedule (PIRS) (Biehl *et al*, p. 68), a revised version of the PIRS called the Behavioural Observation Schedule (BOS) (Atakan & Cooper, p. 78), and the High Royds Evaluation of Negativity (HEN) (Mortimer *et al*, p. 89).

When assessing negative symptoms in practice, there are a number of practical difficulties and potentially confounding factors, as discussed by Johnstone (p. 41). Thus, in patients with schizophrenia it may be difficult to distinguish negative symptoms from depressive features, and drug effects, particularly bradykinesia (Lindenmayer & Kay, p. 108; Barnes *et al*, p. 99; McKenna *et al*, p. 104). Also, negative symptoms may in some cases be a manifestation of positive symptoms (Carpenter *et al*, 1985). For example, a reduction in a patient's level of social interaction may result directly from psychotic disorganisation and a preoccupation with psychotic experiences or as a protective strategy to reduce the degree of external stimulation. Negative symptoms as a manifestation of drug effects or secondary to psychotic phenomena are perhaps more likely to confuse assessment during acute psychotic episodes. This may partly account for the finding that negative symptoms occurring in the acute phase of schizophrenia may differ from those present as persistent features of chronic schizophrenia in terms of their correlations with other clinical variables and prognostic value (Lindenmayer & Kay, p. 108; Pogue-Geile, p. 123; Biehl *et al*, p. 68).

A review of the development of the theories and concepts of negative symptoms is provided by Wing (p. 10). Three papers reflect current views on negative symptoms in Germany (Gross, p. 21; Sass, p. 26; Mundt *et al*, p. 32) which have evolved in the context of a psychopathological tradition somewhat divergent from that in the UK and the USA. The paper by Mundt *et al* also addresses the issue of the diagnostic specificity of negative symptoms. Roth (p. 37) provides a short commentary on the German papers.

Liddle *et al* (p. 119) present evidence for the classification of symptoms in chronic schizophrenia into three subsyndromes, while Crow (p. 15) reassesses the validity of a positive–negative dichotomy, particularly the Type II syndrome. Other papers present data on the clinical correlations of negative symptoms predicted by this concept, that is, the association with abnormal involuntary movements (Barnes *et al*, p. 99; McKenna *et al*, p. 104), cognitive impairment (Liddle *et al*, p. 119) and structural changes in the brain (Andreasen, p. 93).

The relevance and impact of psychological and social variables on negative symptoms are reviewed by Strauss *et al* (p. 128) and the treatment implications of a psychological perspective are discussed by Slade &

Bentall (p. 133). The evidence for a response to drug treatment is evaluated by Kane & Mayerhoff (p. 115).

Despite the evidence for a phenomenological overlap between negative symptoms and other clinical features, and the possible generation of negative symptoms secondary to positive symptoms, the studies and reviews presented in this supplement generally support the existence of a primary deficit syndrome of negative features within schizophrenia. Both the clinical assessment and treatment of negative symptoms remain uncertain areas, but the concept of a negative syndrome has highlighted the need to broaden the outcome criteria used in treatment studies and long-term follow-up studies in schizophrenia to include negative features. Previously, many such studies had restricted outcome measures to relapse of positive symptoms. In addition, awareness of the potential value of negative symptoms in the search for both prognostic factors and clinico-pathological correlations in schizophrenia has been a stimulus for much recent work, and prompted attempts to delineate more precisely the characteristic deficits and residual impairments of chronic schizophrenia. I hope this collection of papers can provide a further impetus to research efforts and clinical interest in negative symptoms, which constitute the most persistent, socially disabling and refractory element of psychopathology for many patients with schizophrenia.

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The Concept of Negative Symptoms

J.K. WING

In a recent edition of the *Schizophrenia Bulletin* devoted to negative symptoms, the editor suggested at the beginning of his preface that what he called the "positive–negative symptom distinction" had been introduced into psychiatry only a decade previously (Levine, 1985). Many authors in the same volume seemed to agree with him; at least they did not emphasise any continuity with earlier work. There were a few notable exceptions. Since, for more than 30 years, I have seen the relationship between psychological deficit (cognitive defect, negative syndrome) and the productive (florid, positive) symptoms as lying at the heart of the mystery of schizophrenia, it seemed possible that some account of how that interest arose and developed might still be timely. This is part of the history of the Social Psychiatry Research Unit of the Medical Research Council.

It is debatable who introduced the 'positive–negative symptom distinction' into psychiatry — it was in the air by the time of Kraepelin's first interest in the subject — but Venables & O'Connor were among the first to operationalise it. A distinction was drawn, on the basis of behaviour scales rated by nurses, between predominantly positive or 'paranoid' and predominantly negative or 'non-paranoid' forms (Venables, 1957; Venables & O'Connor, 1959). Among the residents of the psychiatric hospitals of those days it was easy to demonstrate a syndrome whose central characteristic, statistically speaking, was social withdrawal. Aspects of behaviour such as slowness, underactivity, poverty of speech, lack of interests and poor self-care were highly correlated with social withdrawal, and the total sum of ratings (SW score) was stable over quite long periods of time (Wing, 1959, 1961, 1962; Wing & Brown, 1970).

Also associated but in lesser degree, and subject to much greater fluctuation so that it was not very stable over time, was a syndrome (called 'socially embarrassing behaviour') composed of four elements: overactivity, laughing and talking to self, posturing and mannerisms, and threatening or violent behaviour (SE score).

In addition to these behavioural measurements, a standardised clinical interview was designed to allow the rating of four key phenomena — flatness of affect, poverty of quantity or content of speech, incoherence of speech, and coherently-expressed delusions. This was one of the precursors of the Present State Examination (Wing *et al*, 1967). Among the long-stay schizophrenic group there was a marked and sustained relationship between flatness of affect and poverty of speech rated at interview and the social withdrawal syndrome rated independently by ward nurses on the same patients. A classification was constructed into those who showed none of the four symptoms at interview (1a), those who showed none severely (1b), those who showed only flatness of affect severely (1c), those whose predominant symptom was coherently expressed delusions (2), or incoherence of speech (3), or poverty of speech (4) or muteness (5) (Wing, 1961). Both the classification and the social withdrawal score were highly correlated with other aspects of social performance (Catterson *et al*, 1963).

Group 2, showing coherent delusions without severe incoherence or poverty of speech, always had markedly lower SW scores and rarely had severe flattening of affect, compared with those with other severe disorder. If this group was omitted, there appeared to be a substantial relationship between both SW score and clinical classification and measures of 'arousal' such as skin potential and two-flash threshold (Venables & Wing, 1962).

The particular interest of these ideas for a clinical research worker was that symptoms long thought immutable might well be subject to environmental influence, because there was an underlying psychophysiological mechanism for the interaction. This theory contradicted the concept of inevitable cognitive deterioration in schizophrenia, originating in Kraepelin's early writing on dementia praecox and further pursued by empirical psychologists such as Babcock (1933).

Motivating severely disabled schizophrenic patients

The theory was tested by a design in which controlled social stimulation to improve the work performance of severely disabled schizophrenic patients, allocated at random to two workshops, was brought to bear by two experienced staff nurses, both well known to them (Wing & Freudenberg, 1961). Medication was withdrawn from half of them at random but no ill-effects were noted. After a baseline period during which there was a slow linear improvement on a simple task, paid at piece rates, one of the staff nurses was asked to take such measures as she thought necessary to improve the performance of patients in her workshop. She did so by sitting down next to those who were working slowly or not at all, showing them how to proceed and encouraging them verbally and non-verbally to try. The result was an increase in output from the very first session, but this again did not follow the expected form of a learning curve. (Some patients, however, did not respond at all.) Having reached a peak of about twice the baseline output during the first two sessions, no further change occurred until the staff nurse was asked to stop the active supervision and return to the passive condition. At that point, there was a fall in output to below the level at the start of the experimental period.

In the control group, however, which had continued under the passive condition, there was an initial spurt in output apparently due to the fact that there was an open door between the workshops and patients could hear what was going on in the next room. This was followed in the second session by a dramatic drop in output, which continued until the end of the active supervision next door, when output rose to above the initial level.

After a further period with no active supervision in either group, both supervisors became active, with results that confirmed the earlier findings. Whenever performance improved, 'junk' behaviour (such as aimless pacing or twiddling bits of paper or blankly staring into space) decreased concomitantly. There was, however, no 'transfer of training' — no difference was observable in the behaviour of the two groups when they returned to their wards.

This experiment seemed to demonstrate:

(a) that the stimulation was *social* in nature;
(b) that it resulted in immediate improvement in performance, in some patients, which did not take the form of the expected learning curve;
(c) that the improvement lasted only as long as the stimulation, raising the question of how long it must be kept up. A basic principle of rehabilitation is that passive exercise must be applied until active function returns, otherwise impairment may be amplified;
(d) that stimulation is situation-specific;
(e) that the patients' impairments were at the most severe end of the spectrum and, therefore, that mildly or moderately disabled patients might be less locked into dependence on environmental stimuli, allowing the hope that active function could more readily be restored in some cases.

A comparative longitudinal study of long-stay patients in hospitals providing different social environments

These are large conclusions to draw from one study of the most severely disabled people in hospital at the end of the 1950s. Several other projects were being mounted at the same time, however, which tested a range of hypotheses based on the general theoretical approach. A survey of the long-stay population of two hospitals near London showed that SW scores were correlated with length of stay, as were ignorance of elementary facts about the outside world, absence of plans for the future, and the wish to stay in hospital (Wing, 1962).

The possible reasons for such correlations were examined in an 8 year study of three hospitals, each fully responsible for a geographical catchment area, chosen because their social and rehabilitation policies were markedly different (Wing & Brown, 1961). Analysis of the data, both cross-sectional and longitudinal, controlling for age and length of stay, did nothing to disprove the hypothesis that poverty of the social environment acted on a specific vulnerability to amplify or diminish disablement in people afflicted by schizophrenia.

There was no evidence of any general tendency to deterioration (psychological deficit increasing with time).

Four major conclusions from this large study were as follows:

(a) A core of deficit in many patients is impervious to social influence and constitutes a threat of deterioration if the social environment becomes understimulating.
(b) If this deficit has been amplified in conditions of social poverty, it is possible to reverse the process by making the environment socially more rich.
(c) The effort put into creating an optimal social environment must therefore be sustained because the risk of deterioration remains.
(d) The principles of social treatment would be likely to hold wherever the patients were treated. It could not be assumed that the environment would change for the better simply because a patient had been discharged 'to the community'.

Application to rehabilitation

This theory of schizophrenic vulnerability and reactivity was further tested in pilot research carried out to discover whether such principles when applied to the rehabilitation of long-stay patients would lead to their successful resettlement outside hospital (Wing & Giddens, 1959; Wing, 1960).

The results were sufficiently encouraging to mount a larger study, of 45 moderately disabled long-stay men (Wing *et al*, 1964). Of these, 21 were self-supporting in employment a year later, 10 of them in sheltered work. Three others were employed but their condition was doubtfully satisfactory. In all, 17 patients were living outside hospital. Six patients showed an unmistakable exacerbation of positive symptoms soon after starting a course; none had shown symptoms during the previous 3 months. Five of the six were from a hospital where there had been very little preparation for the new and highly challenging environment they were to encounter. Stone & Eldred (1959) had already pointed out that over-vigorous rehabilitation carried such risks.

A third experiment was carried out later to discover how far chronic psychotic patients, aged under 55 and living outside hospital but unemployed for at least a year, could be helped by attending a course at a newly set up rehabilitation workshop attached to a day hospital where preparatory help could be given (Bennett, 1972; Wing, L. *et al*, 1972). Using the Camberwell Register and case records 75 (44 per 100 000 total population) such patients were identified. There was little improvement in the 14 patients selected at random for the course from the group of 28 who indicated a readiness to take part, compared with controls. Five of these 14 patients had adverse reactions, due mainly to the higher standards of performance required and the pressure to join in group meetings which they disliked, though no harm was done in the long term.

Studies of hostels, group homes, day units and shelters for the destitute have suggested that much less control of the environment is possible 'in the community' than in hospital, although the opportunities for social stimulation generally are richer (Wing & Olsen, 1979).

In the most recent studies of long-term attenders at day hospitals and day centres in the inner London district of South Southwark (Wing, 1982; Brewin *et al*, 1987, 1988; Brugha *et al*, 1988) it has been possible to assess needs for care and for services in the context of resources that are substantially better than in most areas of the country. As is the case with patients at home (Creer & Wing, 1974), the most frequent needs of schizophrenic patients involve negative symptoms and social performance.

Relationship between negative and positive symptoms

One of the social factors liable to precipitate relapse was noted in the second IRU study (Wing *et al*, 1964). This was unrealistic (iatrogenic) pressure to perform up to impossible social and occupational standards, particularly in patients who were quite unprepared for the experience. Another observation, often reminiscent of the same process, was that life changes of various kinds appeared to precipitate relapse (Brown & Birley, 1968). Thirdly, what later came to be called 'high expressed emotion' (most simply operationalised in terms of critical comments made by some key relatives, by no means all) were found to be related to a recrudescence, usually of positive, symptoms (Brown *et al*, 1962, 1972; Vaughn & Leff, 1976).

It became obvious from a 5-year retrospective follow-up study of patients admitted to hospitals A, B and C in 1956 that negative and positive symptoms could occur together or separately throughout the course of most schizophrenic illnesses (Brown *et al*, 1966). This was also found to be true in the World Health Organisation studies (WHO, 1973, 1979; Sartorius *et al*, 1986) in subsequent European studies, and in a controlled trial of preventive medication (Stevens, 1973).

If one studies the vertical hierarchy evident in many diagnostic systems, for example the International Classification of Diseases, there is a progression in the priority given to certain key positive symptoms in the order: organic, first rank, severe affective, anxiety/phobic and obsessional, non-specific. Key symptoms or syndromes higher in the hierarchy tend to be associated with many of the symptoms lower down, but not *vice versa* (Wing, 1978; Wing *et al*, 1974; Sturt, 1981). During recovery from an acute episode of schizophrenia, the key symptoms tend to disappear first while symptoms at lower levels persist longer (Knights *et al*, 1980). Non-specific and affective symptoms tend to recur as prodromal symptoms of relapse (Herz & Melville, 1980; Hirsch *et al*, 1987).

There is an opposite progression in the negative syndrome, which tends to decrease down the hierarchy, being more prominent in dementing conditions, post-encephalitic disorders, parkinsonism and autistic-spectrum disorders (Wing, 1981, 1985) than in schizophrenia. The syndrome occurs at lesser frequency and severity in severe depression and becomes much less evident at lower levels.

These observations suggest that the relationships between positive and negative symptoms in schizophrenia need to be considered in a broader phenomenological and nosological context.

There seem to be at least two environmental processes at work on a biological vulnerability. On the one hand, too little stimulation tends to increase symptoms such as social withdrawal, passivity, inertia and lack of initiative. This process was seen most in the old-fashioned type of mental hospital but it now occurs 'in the community'. On the other hand, there is a tendency to break down, with an effusion of florid symptoms, under conditions of social over-stimulation. This second process is most frequently seen outside hospital but it can also be seen within it. These are general statements and the two processes sometimes vary together. Negative symptoms, in part, are a protective reaction against the disorder of thought and the lack of reward from social contact that ensues because of the communication impairment, and they can, in addition, be amplified in conditions of environmental poverty.

The communication impairment is compounded of several elements, often difficult to separate from each other clinically. There is incoherence of thought and speech, inability to speak to a purpose, a defect of 'willed intention', slowness, and poor non-verbal skill or 'body language'. The same patient may show any of these at various times in the course. An ordered, structured and emotionally neutral environment, providing only demands that can be understood and coped with, but making demands that do exercise real talents, allows the patient to make the best use of assets and compensating skills without amplifying the impairment. On the other hand, if impossible demands are made and the patient is unable to withdraw, the underlying cognitive disorder becomes clinically manifest in productive symptoms and behaviour. The person afflicted by schizophrenia therefore has to walk a tightrope between two kinds of dangerous environment (Wing, 1960; Wing & Brown, 1970; Wing, J.K. *et al* 1972).

Several psychological models have been put forward, each potentially explaining part of this central core of schizophrenia, in which neither positive nor negative symptoms are regarded as 'primary' (Broadbent, 1958; Hemsley & Zawada, 1976; Frith, 1987; Hemsley, 1987). Such models are necessary in order to bridge the gap between the clinical phenomena and the neuropharmacological and neuroanatomical information that is now available.

This assumption of an 'intrinsic' component in schizophrenia does not, of course, rule out 'extrinsic' influences, i.e. factors additional to any psychobiological model that might be constructed. How any disabled person reacts to impairment, whatever its nature, will depend partly on him or her and on circumstances.

In some people with schizophrenia, perhaps 10% according to Bleuler (1978), the disorder is so severe and overwhelming that recovery never occurs. Extrinsic factors mean little in such cases. In 20–25%, recovery occurs within 5 years anyway. In the majority of cases it matters a great deal what the environment is like and those afflicted have to learn to live with schizophrenia much as one might have to live with diabetes or cancer or an amputated limb. This knowledge should be used as the basis for constructing services that will minimise the social disablement of people with schizophrenia and provide them with the highest quality of life possible.

Conclusion

There has been no fundamental discontinuity in the development of theories and methods of investigation of negative symptoms nor of their relationship to positive symptoms. Recently introduced non-invasive methods of examining brain structure and function allow better tests of biological theories and deserve to be exploited to the full. Such preoccupations should not, however, exclude consideration of how putative causes and pathologies may influence the two-way interaction between host and environment. Brain, thought and behaviour can each be isolated and studied in fragments but scientists cannot be satisfied until they understand the links between all three within their social context.

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A Current View of the Type II Syndrome: Age of Onset, Intellectual Impairment, and the Meaning of Structural Changes in the Brain

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Recent interest in positive and negative symptoms in schizophrenia is fuelled by the hope that this dichotomy will identify components with differing prognostic, therapeutic or pathogenetic significance. Correlations have been sought, and some found, in each of these areas. Yet the origin and definition of negative symptoms remain a matter of debate.

In a thoughtful historical commentary Berrios (1984) wrote

> "The old distinction between positive and negative symptoms has of late been reclaimed to describe the symptomatology of schizophrenia. The commonly held view that it originated with Hughlings Jackson is grossly inaccurate. This paper traces it back to J.H. Reynolds and shows current usage to be Reynoldian in that it does not presuppose the complex theoretical model that characterised the Jacksonian view."

In particular Berrios emphasises that the distinction has been used in the recent psychiatric literature not in the sense that positive symptoms are 'release' phenomena secondary to the lesion (which in Jacksonian thinking directly induces the negative symptoms), but with the implication that positive and negative symptoms relate to independent dimensions of pathology.

An attempt by some authors to identify negative symptoms with Bleuler's class of fundamental symptoms gives the issue added significance. Bleuler regarded his category of accessory symptoms (that included delusions and hallucinations now described as positive) as secondary to the fundamental symptoms: therefore his position has a formal resemblance to that of Hughlings Jackson. Yet to regard 'positive' symptoms as now conceived as necessarily secondary to negative symptoms is only possible if one adopts an eccentric view of negative symptoms.

Much depends, of course, on how positive and negative symptoms are to be defined. The distinction was used and developed by Wing & Brown (1970) (see also Wing, this volume) and by Strauss *et al* (1974), both of whom had contributed to the WHO International Pilot Study of Schizophrenia, but it seems to have originated earlier in the Russian literature. Thus Snezhnevsky (1968) wrote that

> "Symptoms that contribute to the different schizophrenic syndromes may be pathologically productive, or so-called positive. Alternatively they may be negative symptoms, expressive of 'flaws', defects and disintegration. Both types combine as a unit, exhibiting organic interdependence and constituting the elements of a syndrome structure ... However although they form a unit, the positive and negative disturbances are not equivalent to each other. In simple schizophrenia as well as in remissions after acute attacks, negative symptoms may sometimes emerge alone without coincident positive ones. I.F. Ovchinnikov (in 1966) has pointed out that the positive and negative symptoms are disposed as if on two levels. The positive is the higher level and is characterised by marked variability ... The lower or negative level by contrast is invariable ... The invariability of the negative disturbances is very clearly demonstrated during contemporary therapy with modern psychotropic drugs. As a result of therapy, the positive disturbances undergo some degree of change and become more rudimentary. In some cases they may disappear altogether, and modern therapy may create a barrier to the emergence of certain features, for instance, of catatonia. The negative disturbances, however, are refractory to therapy and do not change."

Incorporated in this passage are two strands prominent in the recent literature — the notion of positive and negative symptoms as independent variables with differing underlying pathology and time course, and the concept that the negative symptoms are less responsive to neuroleptic medication. Some evidence from our studies at Northwick Park for the latter conclusion was one of the bases of the two syndrome concept that I put forward a few years ago (Crow, 1980).

The two-syndrome concept was an attempt to assimilate the findings of three studies which my colleagues and I had recently completed:

(a) a computerised tomographic (CT) investigation of structural brain changes in chronic schizophrenia (Johnstone *et al*, 1976).
(b) a study of the mechanism of the anti-psychotic effect of neuroleptic drugs making use of the two stereoisomers of flupenthixol (Johnstone *et al*, 1978).
(c) a post-mortem investigation of dopaminergic function in the basal ganglia (Owen *et al*, 1978).

These studies raised problems for the view that underlying the disturbances of schizophrenia is a single pathological change. On the one hand it seemed from

TABLE I
The two syndrome concept (from Crow, 1980)

	Type I	*Type II*
Characteristic symptoms	Delusions, hallucinations, thought disorder (positive symptoms)	Affective flattening, poverty of speech, loss of drive (negative symptoms)
Type of illness in which most commonly seen	Acute schizophrenia	Chronic schizophrenia, the 'defect' state
Response to neuroleptic medication	Good	Poor
Outcome	Reversible	? Irreversible
Intellectual impairment	Absent	Sometimes present
Postulated pathological process	Increased dopamine receptors	Cell loss and structural changes in the brain

the CT scan investigation and our studies of cognitive impairments in chronic states (Crow & Mitchell, 1975; Crow & Stevens, 1978) that one could envisage the disease as a slowly progressive dementing illness of early onset; on the other, on the basis of the flupenthixol study and the post-mortem investigation, that much could be explained in terms of the theory formulated by Randrup & Munkvad (1965) that there is a perturbation of dopaminergic transmission that can be corrected by the receptor blockade induced by neuroleptic drugs. The two syndrome concept suggested that one must accept that there is more than one component to the underlying pathology: perhaps one can relate the more enduring negative symptoms, and the intellectual impairments with which they are closely associated, to structural changes in the brain, and the more readily reversible and drug-responsive positive symptoms to a disturbance of dopaminergic transmission. This concept thus owed much to earlier discussions of the distinction between positive and negative symptoms (particularly in so far as the latter may identify a more enduring component), and attempted to relate this distinction to postulated brain changes.

Definition of negative symptoms

It is important to note that the definition of negative symptoms that we have adopted is more restrictive than that used by many other workers. In our patient studies we have made use of the Manchester scale (Krawiecka *et al*, 1977) (see also Hyde, this volume) for rating schizophrenic symptoms. This is based upon a semi-structured interview and allows ratings on a 0—4 range. It includes delusions, hallucinations and incoherence of speech which we have taken as the group of positive symptoms (although whether incoherence of speech can always be so classified is an open question), and affective flattening and poverty of speech as negative symptoms. Eve Johnstone early modified the scale to allow incongruity of affect to be rated separately from flattening. Experience suggests that these two symptoms often change independently and that incongruity is more closely related to the positive than to the negative group of symptoms.

Some of the problems which have arisen in defining negative symptoms are illustrated by the findings of our trial of the anti-psychotic effectiveness of the two stereoisomers of flupenthixol (Johnstone *et al*, 1978). This study established that the α-isomer is more effective than both the β-isomer and placebo as predicted by the hypothesis that dopamine receptor blockade is necessary for an anti-psychotic effect. We also found that the anti-psychotic effect (as exemplified by the actions of α-flupenthixol) was much greater on the positive than on the negative symptoms as assessed on the Krawiecka scale. The negative symptoms we concluded were relatively resistant to drug treatment.

This conclusion has recently been challenged by Goldberg (1985) who rightly draws attention to the findings of the original NIMH study. In this trial he and his colleagues (Goldberg *et al*, 1965) had shown that drug–placebo differences were seen across a wide range of pathological features, including some which could be described as negative in the sense that a function is diminished or lost.

In our paper we had anticipated this discussion:

> "Improvement in individual symptoms was largely confined to 'positive' symptoms (figure 2 of Johnstone *et al*, 1978). Both non-specific and 'negative' schizophrenic symptoms showed little tendency to improve and no differential response to drug therapy. Thus the scope of the antipsychotic effect may be more limited than was suggested by an analysis of the 1964 National Institute of Mental Health trial (Goldberg *et al*, 1965) in which the benefit of neuroleptic drugs appeared to be as great on some negative *features* of the disease (e.g. social withdrawal, lack of self-care) as on the positive symptoms. Negative *symptoms* (identified in a clinical interview rather than on behaviour ratings as in the earlier study) are uncommon in acute schizophrenia but are prominent in the 'defect state' in which neuroleptics may be less effective."

This point is borne out by the examples that Goldberg gives in his recent paper. Amongst those symptoms which in various trials have been shown to respond better to neuroleptic medication than to placebo he lists indifference to the environment, slowed speech and movements, social withdrawal and poor self-care. Such features are undoubtedly more complex than poverty of speech and affective flattening. The distinction that Carpenter and his colleagues have made between primary and secondary negative symptoms may well be relevant (Carpenter *et al*, 1985). According to these authors some negative symptoms are secondary (in the way that social withdrawal may often be a response to delusions or hallucinations) to positive symptoms or other consequences of the disease. Such symptoms are to be distinguished from primary negative symptoms that are enduring and resistant to treatment.

It is clear that primary negative symptoms do not exist in a vacuum but are related to other features of the disease. For example an association with intellectual impairment was implied by the original two syndrome concept. In the survey of 500 chronic institutionalised patients carried out by Owens & Johnstone (1980) a tetrad (cognitive impairment, negative symptoms, behavioural disturbance and neurological signs) of features was identified that in this population was unrelated to the presence of positive symptoms. This constellation therefore can be considered to represent the features of the defect state or Type II syndrome.

Of particular interest is the presence in this constellation of neurological signs. These include the dyskinesias which are often described as 'tardive' with the implication that they are a late effect of neuroleptic administration. However, such signs were seen before the introduction of such medication (Waddington & Crow, 1988), and are present in patients who have never received such drugs (Owens *et al*, 1982; Rogers, 1985). It is doubtful whether the case that such dyskinesias are sometimes an irreversible consequence of neuroleptic administration has been properly established. Because these movements are more closely related to the longer-term manifestations of the disease than to its treatment it may well be that they should be regarded as a part of the Type II syndrome (Crow *et al*, 1983).

Neurochemical correlates of the Type II syndrome

One possible explanation of the intellectual deficits in chronic schizophrenia is that these patients suffer from some coincidental dementing process e.g. Alzheimer's disease. Against this is the fact that the incidence of cognitive impairments in the population of patients with chronic schizophrenia is well above expectation in the general population (Liddle & Crow, 1984; Buhrich *et al*, 1988). In addition there is no evidence that the Alzheimer disease process is present in the brains of these patients. For example in post-mortem investigations losses of cholinergic and adrenergic neurones (as assessed by the activities of the marker enzymes choline acetyltransferase and dopamine β-hydroxylase respectively) have not been detected (Crow *et al*, 1981). Nor is there any compelling evidence for the presence of gliosis (Roberts *et al*, 1986, 1987).

However, reductions in the content of some neuropeptides have been detected by immunoassay in limbic regions and these losses are found particularly in patients with negative symptoms. Thus losses of cholecystokinin immunoreactivity have been detected in hippocampus and amygdala, and of somatostatin immunoreactivity in hippocampus (Ferrier *et al*, 1983; Roberts *et al*, 1983). Apart from a reduction of cholecystokinin in temporal cortex, changes in these peptides in other areas were not observed, and no alterations were seen in the content of other neuropeptides (e.g. substance P, neurotensin, and vasoactive intestinal peptide) in a number of brain areas. A possible explanation of these findings is that in patients with the Type II syndrome there is a loss of the small interneurones containing the peptides cholecystokinin and somatostatin in hippocampus and amygdala. Of further interest is the observation that cholocystokinin binding sites are reduced in hippocampus, temporal cortex and an area of frontal cortex (Farmery *et al*, 1985), although these losses have not been related to a specific clinical picture.

Two forms of the enzyme monoamine oxidase (MAO) are present in brain — the A form for which phenylethylamine is a substrate, is located mainly in neurones, and the B form, for which benzylamine is a substrate, is found preferentially in glia. In a post-mortem investigation (Owen *et al*, 1987) in schizophrenia, the activity of the A form was unchanged but significant reductions in activity of the type B enzyme were present in areas of frontal and temporal cortex and amygdala. These reductions were seen particularly in patients with affective flattening and poverty of speech. Because of the location of the B form of the enzyme these changes seem unlikely to be related to transmitter function but may indicate some alteration in glial function or number.

The meaning of the structural changes in the brain[1]

Following the early CT scan studies from Northwick Park (Johnstone *et al*, 1976) and St Elizabeth's Hospital (Weinberger *et al*, 1979) a large number of investigations of patients with schizophrenia have been conducted. There is a degree of consensus (e.g. Stahl *et al*, 1988) that when patients with the more chronic forms of the disease are included mean ventricular size is modestly increased. It is also clear that this enlargement cannot be attributed to past physical treatments (Owens *et al*, 1985).

Concerning clinical correlates there is less agreement. While there is a general trend toward finding ventricular size to be related to behavioural deterioration and the more chronic forms of the disease, significant associations with individual features of the defect state are not always found (Crow & Johnstone, 1986). Thus correlations with affective flattening and other negative symptoms, and with intellectual impairment are found in some studies but not in others. In our own recent investigation of over 100 patients with chronic schizophrenia (Owens *et al*, 1985) lateral ventricular size was significantly related to behavioural deterioration and the presence of dyskinesias but not to negative symptoms or intellectual impairment. Although such correlations have been reported in some other studies (e.g. Takahashi *et al*, 1982; Kling *et al*, 1983; Williams *et al*, 1985; Kemali *et al*, 1987) the absence of a consistent relationship is puzzling.

Some light is thrown on this issue by an examination of age of onset as a predictor of outcome and the relationship between brain structure and other clinical features (Johnstone *et al*, 1989). In a population of chronic patients we found that when other relevant variables (e.g. age and duration of illness) were controlled age of onset predicted a number of aspects of outcome. Thus patients who were first admitted to hospital at an age below the mode for the group as a whole (25 years for males and 28 years for females) were more likely than those who were first admitted at a later age to show negative symptoms, intellectual impairment (e.g. age disorientation) and behavioural deterioration. Moreover, some associations between structural change and cognitive function were seen in the early onset group that were absent in the total sample. These correlations were with brain area (that was significantly reduced in these patients by comparison with age-matched psychiatric controls) rather than with enlargement of the third or lateral ventricles.

The findings indicate that age of onset is a determinant of the relationship between the structure of the brain and the cognitive impairments that are one consequence of the schizophrenic disease process. They suggest that these associations are established early in the course of the illness; they are compatible with the notion that the disease itself is an anomaly of development rather than a degenerative process attributable to an exogenous pathogen.

On this basis it might be expected that age of onset would be a determinant of the structural changes in schizophrenia. Surprisingly we found that the three measures (lateral and third ventricular area and brain area) that distinguished patients with schizophrenia from other subjects did not separate patients with early from those with late age of onset. However, a further structural index — the difference between the widths of the two sides of the brain in the posterior segments — did distinguish these groups. Patients with early age of onset had significant ($P<0.01$) reductions in the relative width of the left hemisphere in measures taken in the occipital and temporal regions (Crow *et al*, in press). It seemed from these findings as though early onset of a schizophrenic illness was able to arrest the development of the normal asymmetries which are present in the posterior part of the brain.

This finding may be a clue to the meaning of the structural changes in the brain — that these changes indicate that the core disturbance involves the mechanisms that control the development of asymmetry in the human brain. Some other findings suggest that the structural changes in the brain in schizophrenia are lateralised. Thus in his air encephalographic comparison of acute and chronic patients with schizophrenia Haug (1982) found that the latter had larger temporal horns and that the change was greater on the left side. In their computerised tomographic study of monozygotic twins discordant for schizophrenia Reveley *et al* (1987) found a reduction in CT scan density in the affected twin on the left side of the brain by comparison with the unaffected twin. Such a reduction was not present in non-schizophrenic twin controls. Presumably it reflects an increase in csf spaces that do not appear on the CT image. In a post-mortem study we (Brown *et al*, 1986) found a reduction in width of the parahippocampal gyrus in schizophrenic by comparison with affective patients and this change was significantly greater in the left hemisphere. In a further study (Crow *et al*, 1988) the area of the various components of the lateral ventricle was assessed radiologically after introduction of radio-opaque medium; enlargement was relatively selective to the temporal horn and highly ($P < 0.001$) selective to the left hemisphere. Although temporal horn enlargement was seen in Alzheimer-type dementia this showed no predilection for the left side of the brain.

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[1] See also Andreasen, this volume.

The asymmetries in the human brain are localised in the temporal lobe and include particularly the planum temporale (Geschwind & Levitsky, 1968). They may relate to handedness which itself could be determined by a simple Mendelian gene (Annett, 1985). Thus this gene may be the focus of the disturbance in schizophrenia (Crow, 1984).

Conclusions

A constellation of features that occurs in chronic schizophrenia can be taken as defining the Type II syndrome or defect state. This syndrome is relatively non-responsive to neuroleptic medication and is closely related to the chronic impairments of schizophrenia. These features include (a) negative symptoms (e.g. affective flattening and poverty of speech) relatively restrictively defined (i.e. so as to exclude features that may be secondary to positive symptoms), (b) intellectual impairments, which may be severe, (c) behavioural deterioration, and (d) dyskinesias. The clinical correlates of structural change in the brain have been variable between studies but when present tend to have been among the features of the Type II syndrome. Some evidence from post-mortem investigations suggests that the Type II syndrome is associated with losses of CCK neurones in limbic regions and a reduction of MAO-B (that may be located in glial cells).

Age of onset is an important determinant of the features of the defect state — patients with an early onset are more likely to develop negative symptoms and intellectual impairments than those whose onset of illness is later. It may also influence the relationship between brain structure and cognitive function. Such findings suggest a developmental view of schizophrenia — that the disease is associated with an anomaly of brain growth. According to some radiological and post-mortem findings the focus of the structural change is in the mechanisms that determine the development of asymmetries in the human brain.

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The 'Basic' Symptoms of Schizophrenia

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By concentrating on the apparently uncharacteristic stages in the course of schizophrenia, Huber has drawn attention to subjectively basic symptoms (Huber, 1980, 1983; Huber *et al*, 1979). He has shown in his long-term follow-up investigations of schizophrenic outpatients that uncharacteristic (basic) stages (see below) prevail in the long term when compared with periods of relapse. His new typology of psychopathological outcome underlined these uncharacteristic (purely asthemic) types of remission ("*reiner Defekt*" — Huber 1957*a*, 1961, 1966).

'Substrate-close' basic symptoms

The psychopathology of the basic stages is characterised by manifold dynamic and cognitive deficiencies which are experienced and communicated by the patients themselves as disorders and impairments. The subjectively experienced basic symptoms, elicited by the descriptive–phenomenological method of Jaspers & Schneider, offer a chance to analyse more closely what so-called schizophrenic symptoms may truly be. Huber described them in 1986 as 'substrate-close basic symptoms' because they constitute the primary symptoms of schizophrenia, that is, they are nearer to the hypothesised somatic substrate than the complex psychotic phenomena which are formed and modified by secondary processes. They are termed 'basic' symptoms because they form the basis of a fluctuating productive psychosis (Huber, 1988).

Limbic structures and basic symptoms

Hypothetically, basic symptoms are ascribed to impairments of selective information processing, of lack of hierarchies of habituation and to genetically determined biochemical disturbances in the limbic system ("limbo(thymo)pathy" — Huber, 1971, 1983; Gross & Huber, 1985*a*, *b*). The assumption of a limbopathy and a connection between limbic structures and basic symptoms is supported by the results of neurophysiological, EEG, and psychological investigations (Eroen, 1968; Poljakov, 1973; Huber *et al*, 1979; Hasse-Sander *et al*, 1982). Morhpological alterations in the temporal and diencephalic area of the brain and abnormal rhythms in the EEG point to mesolimbic structures (Huber & Penin, 1968; Penin *et al*, 1982).

Basic symptoms occur in both early and late stages of the disease, and especially in residual states, such residual states can simply be deficiency syndromes, and are often, as Huber stated 20 years ago, an indication of failure; however, they can be almost completely compensated for by favourable environmental conditions. This result was confirmed by the Bonn study (Huber *et al*, 1979).

Phenomenological aspects of the terminology

The phenomenological aspects of pre-psychotic syndromes and prodromes, of post-psychotic reversible basic stages and of irreversible pure defect syndromes reveal a far-reaching overlap. Therefore we have grouped these non-psychotic, untypical manifestations of classic schizophrenia under the term "basic stages in a broader sense" (Huber, 1976, 1983).

Uncharacteristic pre-psychotic syndromes precede the psychotic first manifestation on average by 10 years, last on average 5 months, and then remit completely. Uncharacteristic prodromes last on average 3.2 years, and pass over into the psychosis continuously (Gross, 1969). Post-psychotic reversible basic stages appear immediately after remission of the florid psychotic symptoms. They are differentiated from post-psychotic irreversible pure defect syndromes only when the associated cognitive and dynamic deficiencies persist continuously for less than 3 years (Hasse-Sander *et al*, 1982). Of theoretical and aetiological importance, and also of therapeutic relevance, is that the uncharacteristic basic deficiencies really form the basis of the complex first-rank symptoms. The question is whether the reversible psychotic manifestations are connected with the dynamic and cognitive deficiencies.

Transition states

By follow-up investigations it was possible to prove the existence of psychopathological transition states between basic symptoms and psychosis (i.e. between negative and positive symptoms) and to disprove the objection that such basic symptoms occur in a number of different psychic disturbances. This objection, that basic symptoms are not specific to schizophrenia, overlooks three points:

(a) There are no symptoms specific to schizophrenia: first-rank symptoms are not exclusive as they also appear in organic brain disorders.
(b) The descriptions and definitions of basic

symptoms in the Bonn scale (Gross *et al*, 1987) are characteristic of schizophrenia, especially for the cognitive basic deficiencies — although such phenomena also occur in organic brain diseases; they do not in neurotic or psychopathic personality disorders.

(c) We could prove by follow-up investigations how subjectively experienced basic deficiencies (negative symptoms) can develop into florid psychosis — i.e. into schizophrenic symptoms in the conventional sense.

Thus we can show that it is not tenable to separate so-called positive from so-called negative symptoms or acute from chronic schizophrenia, or a Type I from a Type II syndrome, because all these syndromes are stages of the same disease.

In the last few years our group has investigated systematically, with the Bonn scale, 121 patients. We found 216 transitions from the basic syndromes to florid psychosis (Huber, 19657*a*, 1966; Klosterkötter, 1988; Klosterkötter & Gross, 1988).

We could show that nearly all single cognitive and coenesthetic basic symptoms are primary experiences of psychotic symptoms. For example, disturbances of perception are the basis of delusional perception, and certain cognitive disorders are the basis of acoustic hallucinations. This would support our earlier hypothesis that altered perceptions are very important for the generation of delusional perceptions and misidentification of persons (Huber & Gross, 1977).

The three developmental levels

Basic symptoms can occur in three developmental levels: quite uncharacteristic, (level 1); more or less characteristic (level 2), and, after having undergone modifications by secondary processing, conversion and amalgamation with the so-called 'anthropological matrix', the typical schizophrenic phenomena (level 3). The symptoms can develop from uncharacteristic symptoms (level 1) to somewhat characteristic symptoms (level 2) into productive—psychotic symptoms (level 3) and vice versa. These three developmental levels ('*Entwicklungsstufen*') can then be conceptualised as existing on a psychopathological continuum. The third level, to which level 1 and level 2 basic symptoms may progress in the same patient, also includes Schneider's first-rank symptoms of schizophrenia (Schneider, 1987). As long as no fixation or automatisation takes place in level 3, the development remains reversible; for example, bodily hallucinations (level 3) can revert to coenesthesias (level 2) and to uncharacteristic bodily sensations (level 1).

For the concept of basic symptoms and disorders to be of clinical use, it is important that basic symptoms fluctuate in both their manifestation and degree, depending on given situations, without a discernible cause. Therefore it is only possible by continuous observation to recognise and document the level 2 symptoms, which often occur only in a short and transitory intermediate step before reaching level 3 and corresponding to a higher degree of 'process activity' (Huber & Penin, 1968; Penin *et al*, 1982).

Basic symptoms frequently occur in paroxysms and phases and are released by non-specific everyday situations. In order to acquire more knowledge about basic symptoms in their nascent state and about the relationship between basic deficiencies and florid psychotic symptoms it is necessary to extend the analysis to early and prodromal stages in which the phenomena can most likely be elicited in the original form, not having yet been modified by secondary processes.

Basic stages may show very different degrees of process activity. The so-called pure defect states, the irreversible basic stages, are usually lacking in process activity. The degree of process activity can be determined on the basis of clinically assessed psychopathology. Symptoms in process activity states are, among others, level 2 disorders of cognitive thought, perception, or coenesthetic symptoms, or more characteristic schizophrenic basic symptoms such as vague delusional mood and level 2 delusional perception (Conrad, 1958; Huber & Gross, 1977).

Process activity phases can be correlated, for example, with EEG and neurochemical findings. In phases with a higher degree of process activity the EEG shows abnormal rhythms in the form of alpha-, theta- or delta-parenrhythms, attributable presumably to disturbed functions of the limbic system (Huber & Penin, 1968).

It should be emphasised that basic symptoms are not specific in the sense of being exclusive to schizophrenia. They can also be observed in schizo-affective psychoses and partly in cyclothymic depressions, and even — rarely — in organic brain disease, but not in healthy individuals nor in neurotic and psychopathic personality disorders (Gross 1986; Huber, 1983).

For clinical utilisation of the concept of basic disorders and symptoms it is important that the latter are accessible to the patient's own perception, and also communicable. Most patients are able, in the long term, to view their basic symptoms with critical detachment, to recognise their deficiencies and to develop coping, shielding and avoidance strategies. The patients learn how much strain they are capable of absorbing (socially and professionally) more or less consciously avoiding situations that provoke or intensify their 'negative' symptoms, or even psychotic relapses.

The Bonn Scale

Because of the overlapping psychopathology of the pre-

and post-psychotic reversible and irreversible basic stages, it was possible to construct the Bonn Scale for the Assessment of Basic Symptoms (BSABS) for a standardised documentation of basic symptoms of all pre- and post-psychotic basic stages (Gross *et al*, 1987).

This rating scale is based on the subjectively experienced and reported complaints of 450 patients who had stayed in hospital, at least once in their life, with the diagnosis of schizophrenia and who were re-examined by us by late catamnesis after an average of 22.4 years in irreversible basic stages ("pure residual states" — Huber *et al*, 1979).

In the Bonn Scale the basic symptoms are registered in five main categories and one additional category covering 98 single items. Each basic symptom is defined by means of distinct criteria, commented upon in a glossary, with examples.

The BSABS is a rating scale different from the Frankfurter questionnaire of Süllwold (1983) and the Iowa Scale of Andreasen (SANS). The basis of the Bonn Scale rests upon the complaints and disorders experienced and related by the patients as deficiencies whereas the scale for the Assessment of Negative Symptoms (SANS) is based predominantly on the observation of the patients by the investigator (Andreasen & Olsen, 1982; Gross & Huber, 1985*a*, *b*; Süllwold & Huber, 1986). The Bonn Scale is outlined below, but for greater detail the reader is referred to Gross *et al* (1987).

Two conditions constitute basic symptoms: (a) if the symptoms are not only described as level 1 but also as level 2, that is if they are of special or characteristic quality; and/or (b) if similar complaints disappear during the course of disease.

Direct dynamic deficiencies

The first main category of the BSABS (A), 'direct dynamic deficiencies' (negative symptoms), includes complaints about increased physical and mental exhaustion (A.1) and decreased energy, resilience and perseverance (A.3). Patients complain of physical or mental strain they could cope with quite easily before the onset of the illness; disorders take the form of general weakness, weariness and decreased efficiency. As a direct reaction to these deficiencies patients tend not to allow themselves to make an effort. In contrast to their pre-morbid behaviour they display an inclination to rest; they cease normal activities for hours or even days at a time and sit or lie down frequently.

Indirect dynamic deficiencies

Physical or mental strain can also provoke indirect negative symptoms, such as inner disquiet or tension, sleep disturbances, obsessional thought patterns, coenesthesias, central-vegetative disturbances and lack of concentration. Triggering factors can be physical work in and around the house or the job, sport or such commonplace tasks as dressing or eating. Most frequent causes of mental strain leading to provocation of symptoms include visitors, conversations, or activities that require close concentration, such as reading difficult texts. Patients try to avoid such situations and others like additional workload, problems, or emotional events as these can intensify symptoms.

In the second main category of dynamic deficiencies (B) with indirect negative symptoms, the most important item is increased impressionability (B.2). Everyday events; for example discussions and arguments with others immediately concerning the patients or persons close to them (B.2.2), are experienced more frequently and intensely as insulting, disparaging or offending than before the onset of the illness. The grief and misfortune of others, or fictitious negative information, e.g. crime novels or movies, or memories of the previous disease (B.2.3), provoke indirect negative symptoms, especially obsessive brooding. Such events leave a more intensive and longer-lasting impression than before the illness.

Cognitive thought disorders

The third main category (C.1) deals with cognitive thought disorders. They can be partly summarised under the heading of 'losing control of thought processes' (Huber, 1957*a*, 1961, 1966, 1983).

In interference of thought (C.1.1), patients have intrusive notions that block the current train of thought, leading to increased distraction and loss of attentiveness. Patients try to counter the frequently registered disturbances of concentration (C.1.5) and memory (C.1.8–C.1.11), and the subjectively experienced vacancy of mind or blocking of the current train of thought (C.1.4) by reorganising their work or reducing the speed of it, or by finishing tasks immediately. Patients with disorders of receptive speech (C.1.6) do not entirely grasp the meaning of written or spoken words. In the case of disturbances of expressive speech (C.1.7), the patient may use ingrained speech patterns, and with an increase of such stereotypes a patient's vocabulary can become destitute. This can lead to poverty of speech or poverty of content of speech as Andreasen described in the Iowa Scale (SANS).

Patients with cognitive perception disorder (C.2) complain, for example, about blurred vision, hypersensitivity to light or visual stimuli in general (C.2.3), or about a change in intensity and quality of acoustic perception (C.2.7) resulting, e.g., as hypersensitivity to noises.

Coenesthesias

Coenesthesias (D), the fourth main category, belongs to the most frequent basic symptoms (70%) in all types of reversible or irreversible hypergic basic stages. Coenesthesias predominantly occur as paroxysms setting in with or without external stimuli and lasting for seconds, minutes or hours. Coenesthesia, asthenia and dysthymia commonly occur together and are typical in all basic stages (Huber, 1966). First described as "schizophrenic bodily sensations" by Huber in 1957*a*, *b*, coenesthesias usually concur with decreased vitality ('asthenia'), and show a phenomenal similarity to spontaneous sensations of the thalamus (Huber, 1957*b*). Coenesthesias can, over short periods, fluctuate in intensity, sometimes becoming intolerable and even leading to suicide. The special experience suffered from these bodily sensations is connected with the difficulty of describing these sensations.

Diagnosis and treatment

Until the present time a comprehension of basic symptoms was neglected, although they are very important for early diagnosis and early and adequate treatment. The therapy (psychopharmacological as well as psychological training methods) has to be centred upon the various inter-individual basic deficiencies. It should thus be possible to impede any increase of cognitive basic symptoms and disorders in prodromes and pre-psychotic syndromes before the transition to schizophrenic psychotic symptoms. Here we have to consider that the capacity to experience and communicate the basic symptoms, the ability to maintain insight and still be able to cope with the basic deficiencies diminishes with increasing process activity of basic symptoms.

The susceptibility to breakdown under certain critical conditions, e.g., large workloads, emotional stimulation or a change in everyday situation, which strain the patient's information-processing capacity, causes a decrease in the patient's efficiency. On the other hand it allows the understanding of reactions and behaviour that at first seem incomprehensible to observers, and threatening to the patient himself (Huber, 1983; Süllwold & Huber, 1986).

Our results support the hypothesis that long-term prognosis is more favourable and complete remissions more frequent if an adequate therapy commences as early as possible, preferably in the prodromal stages (Gross *et al*, 1983; Huber *et al*, 1979).

The results of the Bonn study show that the patients are able to overcome psychosis but less so, or not at all, the basic symptoms which persist after remission of psychotic episodes and constitute the basic stages. Withdrawal (secondary autism) is very often a consequence of the patient's effort to cope with the basic symptoms, at least partially and/or to avoid situations which can precipitate or increase basic symptoms including provocation of and/or transition into productive psychotic symptoms. The risk of deterioration and intensification of basic symptoms and provocation of psychotic relapses by triggering factors can be mitigated through a combination of neuroleptic treatment and rehabilitation regimes adequately structured with respect to intensity and quality of the basic symptoms (Huber, 1983; Süllwold & Huber 1986; Gross *et al*, 1987).

If we want to find the fundamental disturbances in schizophrenia we have to abandon some of our conventional ideas, e.g. that the whole personality of schizophrenics is always affected in contrast to patients with organic brain diseases; that schizophrenic patients have no ability to perceive their deficiencies, cannot maintain a critical distance to them and are unable to cope with, adapt and compensate for them. Over the long term, the majority of schizophrenic patients do not present with typical psychotic phenomena; instead they show basic stages which are different from the 'conventional' schizophrenic syndromes. Basic stages manifest more as a failure of efficiency than as a change of personality. This implies that the ability to work and have social contacts is impaired, whereas, for example, legal responsibility is maintained. The concept of basic symptoms therefore is of considerable importance for the treatment and the proper social appreciation of the phenomenon of schizophrenia (Huber *et al*, 1979; Huber, 1983). The standardised documentation in the Bonn Scale of the basic symptoms is important therefore for therapeutic strategies and rehabilitation programmes and especially for prevention, early diagnosis and early treatment.

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The Historical Evolution of the Concept of Negative Symptoms in Schizophrenia

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The concept of negative symptoms is rather tempting for those who theorise on psychiatry. It corresponds to a strong tendency to subtyping, it simplifies a variety of complex theories of schizophrenia and it aspires to the integration of descriptive phenomenology, clinical/psychopathological knowledge, and neurochemical, anatomical and pathophysiological data. A concise and influential example has been the two syndrome concept of Crow (1980) (see also Crow, this volume), which was modified in 1985, and in which, surprisingly, both Bleuler and Pinel-Haslam are declared the forefathers of the positive and negative forms of schizophrenia. This review concentrates on the historical roots of the concept of negative schizophrenia from the viewpoint of psychiatry in German-speaking areas. This corresponds with the ideas of Strauss (1985), who called for more study of the psychological processes described by pioneers in the field, for example concepts as 'will' and 'energy'. Such historical study also seems to be useful with respect to the considerable variety in concepts and terms that gradually developed in the field of so-called positive and negative schizophrenia (Table I).

In everyday clinical practice these terms are often chosen rather intuitively. Some of them overlap, some have a causal relationship, and often they are used more or less synonymously, even if none of them has a generally recognised definition. It is unclear which considerations are decisive for allocation of a symptom to the positive or negative category.

TABLE I
Current dichotomies for symptoms, syndromes or subtypes in schizophrenia

I	*II*
Positive	Negative
Acute	Chronic
Plus	Minus
Secondary	Primary
Accessory	Fundamental
Productive	Deficient
Hyperphase	Hypophase
Florid	Poor
Active	Residual

Origins of the concept in English-speaking psychiatry

In Great Britain there has been controversy over whether the division of schizophrenic symptoms into positive and negative forms has its origin in the writings of Jackson (1889), (see Crow, and also Andreasen, this volume) or those of Reynolds (1858), or was first used explicitly in a psychiatric context by de Clérambault (1942) (Berrios, 1985). Jackson assumed a hierarchical–evolutionary model of the mental apparatus, in which negative symptoms were caused by a loss of normal functions and abilities. These symptoms represent the positive elements; they are secondary disinhibitory phenomena or deformations and exaggerations of normal functions. In contrast to Jackson, Reynolds started with energetic ideas of an excess or lack of the vital tonus.

Trimble (1986) pointed out that Jackson is in better congruence with the present aspects in schizophrenia research than Reynolds. Jackson's starting point of an organic brain damage seems to correspond with some modern biological results of brain dysfunction in schizophrenia. Moreover, Reynolds considered the positive and negative symptoms as being independent of one another, while they were combined in Jackson's theory. Reynolds' views are of interest because a clearly vitalistic approach plays a special role in past and present German-language theories of schizophrenia, and such an approach involves conceptions of psychic energy and dynamics.

Insufficiency theories of schizophrenia

The constructs of mental energy, vital tonus, and affective dynamics have had considerable influence on the theories of insanity and schizophrenia. Insufficiency and deficiency became more and more influential. Various insufficiency theories are listed in Table II; however, only some of them can be detailed here. Since the turn of the century, the Viennese psychiatrist Berze published a number of clinical and theoretical reports on paranoia, mania, and schizophrenia. His differentiated concept of schizophrenia is schematically described in Table III.

Like most psychiatrists of his epoch, such as Kahlbaum, Kraepelin, Bleuler, Jaspers, Carl Schneider and Kurt Schneider, Berze assumed that the cause of dementia praecox was a pathological process in the brain. He worked out the basic psychotic disturbance in schizophrenia, which can be regarded as the psychopathological equivalent of the organic process and

TABLE II
Insufficiency hypotheses of schizophrenia

Griesinger	(187f)	Weakness-state of insanity with reduced energy of mental life
Kraepelin	(1893)	Development of chronic weakness-state dementia praecox
Janet	(1903)	Abaissement du niveau mentale
Bleuler	(1911)	Loosening of associations
Kleist	(1913*a*, *b*)	Disturbance of activating
Berze	(1914)	Primary insufficiency of psychic activity
Conrad	(1958)	Reduction of energetic potential
Janzarik	(1959)	Dynamic insufficiency
Huber	(1966)	Fundamental cognitive disturbance and basic deficiency

summarised it as a primary insufficiency of mental activity (1914); later he modified the concept as hypotony of consciousness (1929). The so-called primary or process symptoms of schizophrenia directly stem from the basic psychotic disturbance. Moreover, the process can lead to lesions in the brain and, as a consequence, to defect symptoms, which outlast the active process. So, in a longer lasting illness, the primary, specifically schizophrenic phenomena within the symptomatology can mix with post-process symptoms caused by organic changes. In a life-long course, the secondary features can take precedence over the primary symptoms or even displace them; on the other hand (according to Berze) a new exacerbation of the organic process can always cause a reappearance of the primary symptoms.

For Berze, a clear distinction between process symptoms and defect symptoms is necessary for a psychological theory of schizophrenia. Berze answers the decisive question of the criterion for this differentiation of primary and secondary (active and defect) psychosis by a subtle psychopathological analysis. He emphasises the importance of the initial disease and, as an indication of the initial process, he tries to find out whether a sympathetic understanding of the patient's psychic phenomena can be achieved by intuition. Thus, Berze employs the phenomenological method, which goes back to Husserl and Dilthey and which at that time was introduced into psychopathological research by Jaspers (1913). This meant a deliberate extension of the descriptive approach of Kraepelin who, in several editions of his textbook, had gathered more and more details of symptoms. However, Berze did not concentrate on unconscious motives and contents, as did Bleuler & Jung (1908) for schizophrenia with their theory of affect-loaden complexes. The phenomenological psychopathologists used empathy and introspection to reconstruct the experiences of the patient in order to subject his motives, reflections and feelings to a formal analysis.

So Berze's distinction of primary and secondary, of acute process and of defect symptoms, was done by psychological means and the way the individual phenomena developed from one another with internal plausibility was heuristic. Chronology was of special importance. Berze's ideas, which largely defy a concise operationalisation, cannot be quoted in detail. One example is his analysis of thought disorders. He pointed out that the results of an 'external' examination are not

TABLE III
Berze's theory of schizophrenia (1914, 1929)

Initial organic process

↙	↘
Fundamental psychotic disturbance (primary insufficiency of psychic activity)	Lesions of brain tissue
↓	↓
Schizophrenic primary symptoms (symptoms of active process psychosis)	Secondary symptoms of inactive schizophrenia (defect symptoms)
primary thought disorder (incoherence)	secondary thought disorder (bizarre thinking)
primary hallucinations	hyperfunctioning (negativism, chronic delusion, mannerism, stereotypy)
alteration of the sense of activity	
specific schizophrenic alteration of basic feeling (Grundstimmung) feeling of insufficiency (Wahnstimmung)	hypofunctioning (lack of interest, monotony, emotional flattening)

sufficient, as it only registers disturbances of performance and affect. More important is the 'internal' examination, which, from the phenomenological viewpoint, considers both the subjective experience and the altered relationship of the ego to the experience. Some of the criteria for the analysis of thinking are patterns of thought order, attentiveness, passive sticking to contents, quantitative increase with qualitative devaluation of thoughts, and actualisation of peripheral contents.

According to Berze, incoherence is a primary schizophrenic thought disorder. It is registered by the patient subjectively: he feels disturbed and handicapped, sometimes helpless or perplexed, occasionally with delusional interpretations of the changed experiences. So the initial process, the primary symptom of incoherence, is both objectively and subjectively disturbing. Contrary to this, the secondary defect symptom of schizophrenic thought disorder, e.g. bizarre thinking, is a phenomenon which in most cases can only be registered objectively. The patient himself considers his strange ideas, thoughts and arguments as rational. A self-confident security has often replaced the perplexed insecurity that had been the reaction to primary incoherence.

The next process symptoms are the primary hallucinations, which are also considered as a direct expression of the fundamental disturbance. Berze emphasises that hallucinations occur in combination with other diseases and also with many inactive schizophrenias, neither are to be considered as primary, but they result from secondary changes, firstly from disturbances of association. The primary hallucinations have an explicitly sensory quality, and they are genuine hallucinations, whereas the secondary ones, according to Berze, are often pseudo-hallucinations.

The third primary symptom for Berze is the disposition to changes in the consciousness of activity, an aspect which is of decisive importance for the first-rank symptoms of Kurt Schneider (1959), here however with a slightly different meaning.

Further primary symptoms are certain forms of thought withdrawal and blocking as part of a comprehensive schizophrenic disturbance of self-experience. The last primary symptom of Berze is a schizophrenic basic mood, involving complex alteration composed of many psychic events, principally paranoia, estrangement, change and a general experience of insufficiency.

Association-psychological theory of schizophrenia

Eugen Bleuler's theory of schizophrenia is mentioned only briefly, because it is well known and influential in Anglo-American psychiatry. However, this theory might have caused some confusion as it differentiates, in a somewhat complicated manner, basic symptoms and accessory symptoms on the one hand, and primary and secondary symptoms on the other. The negative symptoms of the present terminology are seen in a narrow reference to Bleuler's essential or basic symptoms, e.g. by Pfohl & Andreasen (1986). Their identification is rightly challenged by Crow (1985). In Bleuler's two-fold differentiation of schizophrenic symptoms, the first group is specified clinically by course. Disturbances of association (affect, ambivalence, and autism) are said by Bleuler to be always present; the accessory symptoms (hallucinations, personality disturbances, mania and catatonic signs) occur only during severe relapses.

The second differentiation is based on an aetiopathogenic hypothesis; Bleuler describes primary symptoms as the direct consequence of the assumed organic process, such as some disturbances of association, numbness, disposition to hallucinations, vegetative disturbances and catatonic symptoms. With reference to the psychoanalytical ideas of Freud, reactions of the insane psyche were considered as secondary symptoms, occurring as a result of a more or less unsuccessful adaptation to the primary symptoms, such as fragmentations of thinking, symbolisations, disturbances of affect, memory and orientation, automatism, delusions, autism, abulia, and negativism. Bleuler's distinctions stimulated important theoretical discussions and research (see Berner & Küfferle, 1982) but they were often misinterpreted, for example being confused with the first- and second-rank symptoms of Kurt Schneider (1959).

Criticism of association psychology and pure deficiency hypotheses

The psychiatrist Hans Walter Gruhle was clinically influenced by the traditions of Kahlbaum and Kraepelin, while methodologically he followed the phenomenology of Jaspers. He astutely and critically looked at the theoreticians of schizophrenia of his period, such as Kraepelin, Bleuler, Kretschmer, Carl Schneider, and Kurt Schneider, and especially Berze, with whom he published a monograph about the psychology of schizophrenia (Gruhle, 1929). Regarding Kraepelin, Bleuler and Jung, he criticised the close relationship with the association psychology of Wundt, which led the attention to the schizophrenic disturbances of thought and associations. The observation of psychic acts, the functions of consciousness and self, the motives and intentionality, were psychologically new aspects in the writings of Jaspers as well as Berze and Gruhle. Additionally, the viewpoint of the vital tonus and -dynamics once again became significant, which is decisively important for the theory of negative schizophrenia.

In his criticism of Berze, Gruhle (1929) touched on an important disadvantage of all conceptions about schizophrenia, which are based on a pure insufficiency theory. When, for example, Bleuler assumes a loosening of the associations, or Berze a primary insufficiency of psychic activity as psychotic basic disturbance, an element of 'minus' is made responsible for the schizophrenic symptoms. According to Gruhle, both authors get into difficulties with their theories with respect to the 'positive' symptoms, such as intense affect or catatonic excitation. The explanations of 'hypo' are not sufficient for most of the 'new' symptoms of schizophrenia. In this context, Gruhle (1922) used arguments which anticipate some of the present-day discussions: "It seems undeniable to me that in many cases of dementia praecox there is a *plus* of impulses. Similar to the occurrence of sometimes a *hypo-*, sometimes a *hyper*-phase in the manic-depressive insanity, which today is considered as unity, some courses or phases of schizophrenia distinguish by a *plus*, others by a *minus* in mental activity."

Gruhle (1929) considered both the hyper- and the hypofunction as being psychologically inexplicable, primary symptoms. Thus his theory of schizophrenia is based on the concept of a fundamental disturbance containing two essential elements: a disturbance of the intentional motives as a qualitative factor and a disturbance of mental activity as a quantitative factor.

In view of the ubiquity of schizophreniform symptoms, Gruhle regards subjective experiences as being specific to schizophrenia, and this is in line with the phenomenological school and with Berze. Gruhle also assumes the existence of primary symptoms, caused directly by the schizophrenic process. For the patients, they are, at least initially, characterised by the impression of something strange, inspired, or imposed, whereas the examiner sees them as underivable, incomprehensible, and without sufficient motive. Primary symptoms in this sense are some genuine hallucinations, schizophrenic basic mood, abnormality of impulses, thought disturbances, and primary delusions. Concerning the dichotomy positive versus negative, Gruhle judges negative symptoms as being similar to those belonging to the current deficient form, i.e. flattening of thought, stereotypes, perseveration, apathy, and abulia. Gruhle points out that numerous symptoms are not suitable for the classification into negative and positive, such as active negativism or autism, which can be very variable.

Dynamistic theories of schizophrenia

The next important representative of energetic or dynamistic schizophrenia theories in German psychiatry is Klaus Conrad (1958), who was influenced by the organo-dynamic conceptions of Henry Ey and, consequently, by the theories of Jackson. Ey (1963) adapted the model of an evolution of mental functions and its gradual disintegration into mental disturbances, which leads to a regression to former strata and functions. Diseases do not produce any new psychic phenomena, but only release phylogenetically older features: the negative process of decomposition and of loss can produce positive aspects by the release of active functions. Conrad connected this model with ideas of structural psychology, Gestalt psychology, and neuroanatomy. His subtle analysis of the changes of the Gestalt in the early phases of schizophrenia led him to the basic principle of a reduction of the energetic potential, to which, however, Gruhle's criticism of the one-dimensional energetic explanation pattern applies.

In the dynamistic approach there are close connections between the schizophrenia theory of Conrad and the structural dynamic conception of Janzarik (1959, 1968). As it cannot be easily outlined in the English language, because of its difficult terminology, we follow a description from Berner & Küfferle (1982):

> "The term of psychic structure contains pre-programmed behavior patterns and intellectually constructed inborn or acquired representations. The corresponding term of dynamics is devoted to a fundamental level of affectivity, drive and emotionality. In florid psychotic disorders three specific dynamic derailments occur: dynamic expansion, typical for manic states; dynamic restriction, typical for depressive states; and a rapid fluctuation between these forms which is called dynamic instability. In poor-prognosis-schizophrenia Janzarik describes a dynamic depletion characterized by clinical states of affective flatness and loss of drive."

It is interesting that since 1959 the structural dynamic approach has distinguished between a dynamic derailment of the instability type, whose productive phenomena respond well to neuroleptic drugs, and a dynamic insufficiency, which is practically inaccessible to somatic therapy (Janzarik, 1987). It is easy to see how these psychopathological and psychopharmacological considerations of a dynamistic approach correspond with the current distinctions in positive and negative symptoms.

Janzarik's theory of schizophrenia contains an additional and rather unusual hypothesis, formulated as the 'paradox of preexisting deficiency' (1959), which is of interest for the aetiology of negative forms of schizophrenia. He assumes certain dynamic weaknesses in the premorbid personality, which can be discovered in the critical phases of productive psychotic derailments. For Janzarik the apathy syndrome that remains after a relapse is often no more than a mild dynamic insufficiency already inherent in the patient's character prior to the onset of the disorder, so that, in his view, much of what has been ascribed to the pathological process in the manifestation and development of schizophrenic syndromes might be rooted in the personality of the patient (Janzarik, 1987).

The advantage of the dynamistic conception by Janzarik compared with the one-dimensional deficiency hypotheses of schizophrenia is the more precise differentiation of the dynamic conditions, which are composed out of the four principal dynamic constellations. From this, the variety of schizophrenic symptomatology with the transitions and overlappings of positive and negative phenomena can be derived in a more plausible way than is possible by a simple division into positive and negative forms. However, Janzarik's conception includes an equally important structural aspect, which is supplementary for the interpretation of schizophrenic disorders, but which cannot be dealt with in detail here.

Summary

Table IV schematically summarises the models of some important theoreticians in order to indicate the heterogeneity of the conceptual basis for the distinction between positive and negative forms of schizophrenia. Thus, in different terminologies, positive and negative symptoms by Reynolds and Jackson are related to different mental and somatic disturbances. Bleuler mainly judges associations and their possible alterations, particularly by affect. When Berze, through the insufficiency of mental activity, places a negative element into the centre of his schizophrenia theory, he is interested in the conscious mental acts and intentionality. Gruhle, on the other hand, considers the different activity of hyper- and hypo-phases and, as an additional dimension, the comprehensibility of motives. Janzarik, in his dynamistic conception, first of all analyses the positive and negative conditions from the viewpoint of energy and emotion. This simple review advises caution when composing historical positions to a unitarian concept of positive and negative psychoses.

Considering the present discussion, however, we find a similar situation with quite different areas, which serve as support for the division into a positive and negative form of schizophrenia. The logic of these tendencies corresponds with the present trend to a multiaxial or multidimensional registration of clinical, psychopathological and biological data. However, the various levels of explanation have questionable relations to each other. According to the clinical model based on natural sciences, we expect an approach to valid entities by an optimisation of the defining criteria which are derived from psychological, somatological and clinical sources (Sass, 1987). The simplifications necessary when collapsing the heterogeneous data in two subtypes are in opposition to the psychosocial complexity of mental disturbances and their courses. The original positive/negative division is not always sufficient.

Examples are the differentiation of type-A and type-B negative symptoms by Pogue-Geile & Harrow (1985), and the clinically valuable description of transitory and pure forms of negative symptoms by Carpenter *et al* (1985). They have argued that symptoms which seem to be negative can result in different ways from

TABLE IV
Conceptual roots for the distinction of negative and positive forms of insanity

Author	*Theoretical background*	*Main area of investigation*	*Explanatory model*
Reynolds (1858)	Vitalistic	Psychic + somatic phenomena	Negative: negation of vital properties Positive: excess of vital properties
Jackson (1889)	Hierarchical–evolutionistic	Psychic + somatic phenomena	Negative: loss of functions Positve: increased automatic action
Bleuler (1911)	Accociation–psychology	Thinking + affects	Negative: loosening of associations Positive: reactions of sane mind
Berze (1914, 1929)	Dynamistic, act-psychology	Psychic activity + intentionality	Negative: insufficiency of psychic activity Positive: loss of intentional control
Gruhle (1922, 1929)	Dynamistic, motivational analysis	Psychic activity + motivation	Negative: primary hypophases Positive: primary hyperphases
Janzarik (1959, 1968)	Dynamistic, structural psychology	Drive + emotion, psychic structure	Negative: dynamic insufficiency + depletion Positve: dynamic expansion + instability

productive psychotic phenomena or even from a treatment directed against them.

Of similar importance is an aspect which already became evident in the discussions by Berze and Gruhle: apparently positive symptoms would be the consequence of negative phenomena and functional deficiencies. An overproductivity must not necessarily be an indication of an increased activity, but can also be a consequence of insufficient functions of organising and integration (Berze, 1929). Thus, at least as far as psychopathology is concerned, it is reasonable to doubt whether the symptoms occurring in schizophrenia can consistently be divided into a positive and a negative group.

A final aspect derived from the historical analysis is the question whether, besides the plus/minus dichotomy, the differentiation of primary and secondary psychological phenomena of schizophrenia should be picked up with similar intensity. This could be important for the adequate treatment of heterogenous secondary symptoms, as Carpenter *et al* (1985) have shown. Additionally the delineation of primary symptoms in the initial phases of schizophrenia can also be crucial for biological research and for the theories of schizophrenia.

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The Diagnostic Specificity of Negative Symptoms and their Psychopathological Context

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Rating scales for negative symptoms, basic symptoms and other comparable psychopathological syndromes were not originally constructed in order to make psychiatric diagnoses. Moreover, these scales were intended to be applied principally to schizophrenic patients. From the point of view of psychological testing their application to non-schizophrenic patients could be rejected on methodological grounds. Nevertheless there are some considerations which may justify such an investigation.

First, comparing negative symptoms in schizophrenic and non-schizophrenic patients and examining the overlap which can be expected may reveal some aspects of the psychopathological structure and strata of the negative syndrome. Second, negative symptoms have recently been correlated to biological variables as possible 'markers' of 'negative schizophrenia' as opposed to 'positive schizophrenia'. If it turns out that negative symptoms cut across a number of psychiatric diagnostic groups, it should be difficult to extract a specific schizophrenic trait marker using these negative symptoms.

So far, a few studies have demonstrated that the negative syndrome is not specific to schizophrenia. Nestadt & McHugh (1985) examined a large general population and found that negative symptoms as measured by the Scale for the Assessment of Negative Symptoms (SANS) were most frequent in schizophrenics but also occurred often in major affective disorders and organic states with dementia or delirium as well. They occurred to a lesser degree in neurosis, personality disorder and phobia, and even 7% of the psychiatrically healthy individuals displayed at least one negative symptom. In the German literature there are several studies dealing with the specificity of basic symptoms as measured by the Frankfurter Beschwerde-Frageboden (FBF) (Süllwold, 1977). This self-rating scale incorporates fluctuating cognitive microsymptoms. All authors using the FBF have found that basic symptoms occur as often in diagnostic groups such as neurotics, prisoners, organic states, as in schizophrenics.

Method

In our study we examined negative symptoms and some very similar psychopathological syndromes in four diagnostic groups, each containing 20 patients: schizophrenia, endogenous depression, neurosis, and diabetes mellitus; the latter is a non-psychiatric illness with a chronic character, a certain degree of social handicap and to a certain degree a compliance-based course. The diagnoses were made according to ICD–9 and reassessed according to DSM–III. Most of the schizophrenic patients constituted a group demonstrating a mild residual state cross-sectionally with occasional relapses to productive symptoms. The neurotic group had a number of different diagnoses, most of them presenting with anxiety syndromes, neurotic depressions and some personality disorders after a more acute episode. The duration of illness had to be 5 years or more, and the patients had to be between 35 and 55 years of age. Two trained psychiatrists examined the patients shortly before their discharge from the ward, when the acute symptoms had ceased and negative symptoms could be expected to be present.

This paper will report the results with four of the psychopathometric instruments we used. Three of them greatly overlap and cover parts of what might be called the schizophrenic defect state. The SANS is internationally known and needs no explanation here. The construct of the Inteltionalitätsskala (InSka) (Mundt *et al*, 1985) is orientated towards the patient's degree of ability to constitute interpersonal reality as, for example, in the common meaning of a word, of an affect of a cognition. The FBF (Süllwold, 1977) is a self-rating scale primarily focusing on phenomena referable to slight derealisation and cognitive gliding (here called 'basic symptoms') (see also Gross, this volume).

The Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie (AMDP) (Baumann & Stieglitz, 1983) with its 'apathy' profile represents a comprehensive collection of psychiatric symptoms very similar to those in the IMPS. Ch. M. and S.K. did the rating. The inter-rater reliability ranged from 0.6 with the AMPD to 0.73 with the InSka. For statistical analysis the mean values of the two raters' data were used. The diagnostic groups were compared by means of Kruskal-Wallis Tests, with the alpha-adjustment.

Results

All the SANS subscores as well as the total score range were highest in the schizophrenic group, but statistically significant separation between schizophrenics and one of the other psychiatric groups was evident only on the Alogia subscore at the 1% level, and on the Affective flattening subscore at the 5% level. The most impressive, almost bimodal, separation is shown in the graph on the Alogia subscore, whereas Apathy, for example, demonstrates great overlap (Fig. 1).

A strikingly similar situation occurs with the InSka (Fig. 2). This scale succeeds in significantly separating the diabetics as well as the other two psychiatric groups from the schizophrenics, except on the subscores for Motor activity and Initiative. It seems remarkable that in both the SANS and the

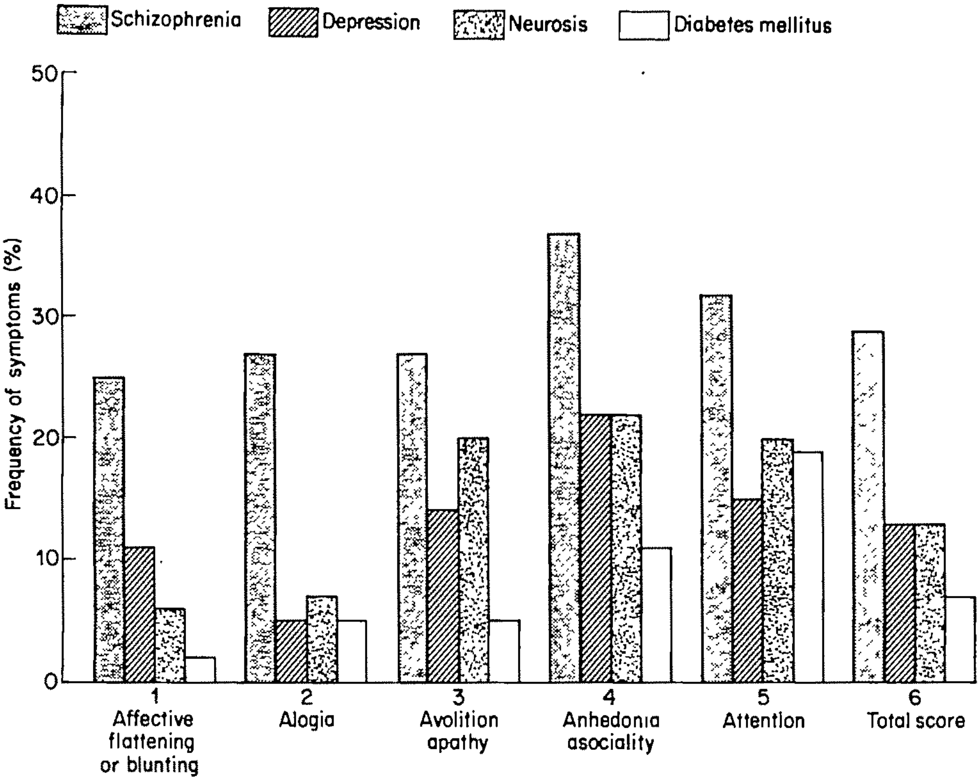

FIG. 1 SANS: Subscores and total score of each diagnostic group.

InSka, the language subscores apparently do best in separating schizophrenics from the other diagnostic groups.

The self-rating scale FBF performed in a totally different way. In this case the highest values on subscores and total score were achieved by the neurotic patients, although significant differences occurred only between neurotics and diabetics. Even those subscores which are considered essential for the theory of basic disturbances, namely Cognitive gliding and Loss of automatisms, demonstrated the highest ratings in neurotic patients.

Since both the InSka and the SANS seemed to be the most specific to schizophrenia with respect to their language subscores, we compared those subscores of the four instruments which reflect language and language behaviour with comparable items (Fig. 3). It turned out that using the SANS, the InSka, the AMDP apathy profile (which refers grossly to language behaviour) and also the FBF results in very similar ratings for language disturbances in schizophrenics in the range of about 30% for positive answers, while the neurotics in FBF score much higher — 60% — than do the other groups. Thus, one must conclude that the discrepancy on the language subscores between the self-rating scale FBF and the other instruments is not due to low scores in the schizophrenics when self-rating, but due to high scores in the neurotic patients. In other words, this means that a deficiency in self-perception of the schizophrenics does not seem to be playing a role here. However, it is still uncertain how the higher scoring of neurotics on the self-rating scale can best be interpreted.

To arrange all the subscores of our instruments in an order best reflecting their diagnostic accuracy we used χ^2. Because of the different group size between schizophrenics (20) and non-schizophrenics (60), the Youden-Index was used; its maximum served as a cut-off point for separation of the groups. A discriminant analysis was not done because of the ordinal character of our data (Table I). Once again the language subscores and Autism and Delusion scores on the InSka do best according to this accuracy measure; they do nearly as well as Motor Activity and AMDP Apathy, the latter also describing language behaviour. The bottom half of the rank order contains subscores describing the psychopathology of withdrawal, affective flattening, loss of motivation.

If we move on to the level of single items and leave aside the Autism and Delusion items of the InSka which cannot be taken into account in this instance since they contain positive symptoms in the sense of SANS, three language items again do best.

A correlation matrix with Spearman's r of all subscores in the schizophrenics and the non-schizophrenics reveals some differences between the intercorrelation patterns of these groups. Three InSka subscores can serve as an example (Table

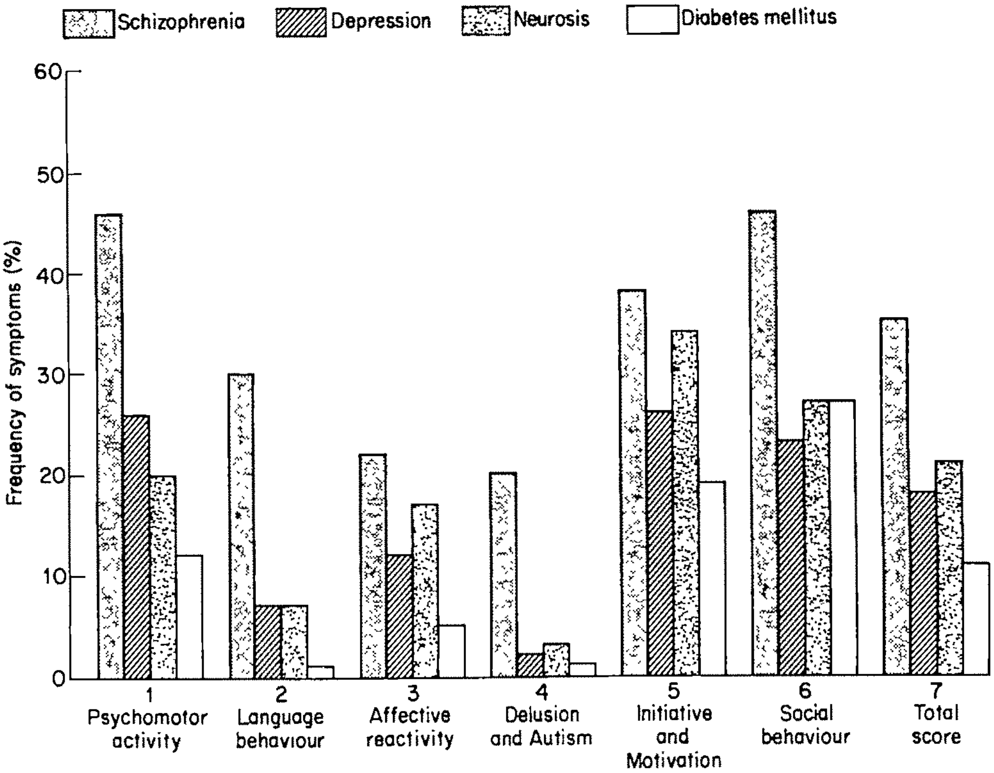

FIG. 2 InSka: Subscores and total score of each diagnostic group.

II). Affective reactivity has a high Spearman's r value with Language behaviour in the group of schizophrenics but not in the non-schizophrenic group; in the latter, however, the correlation between Affective reactivity and Initiative and Motivation is high. The same applies when looking at the subscores Language behaviour and Psychomotor activity. From this finding one may conclude that a certain psychopathological syndrome can be of a different nature according to the manner in which it is embedded in other psychopathological phenomena. Taking Affective reactivity as an example, it might be that its pathology in neurotics is due to lack of motivation, withdrawal and resignation — a developed personal attitude — whereas its pathology in schizophrenics may be due to language disturbances which include pathology of thinking and perception, a difference which may reflect a different pahtogenesis for the psychopathology of this subscore Affective reactivity. In other words, the negative syndrome could be at least two-fold, comprising one fairly elementary feature predominant in schizophrenics and one more reactive feature prevailing in neurotics and depressives.

Emphasising some aspects of the factorial structure of InSka will bolster this argument further. This structure may reflect the psychopathological complexity of the negative syndrome and this is what the scale is meant to describe. The following is based on data from another study (Huerkamp, 1987) which attempted to validate the InSka on over 100 schizophrenics with a mild residual state who had each been independently assessed with the InSka by three to five psychiatrists.

The InSka consists of six subscores; in all there are 60 items. Answers are to be given on a Yes-No dichotomy. Factor analysis systematically re-examined the original six-factor structure of the InSka which guided its construction, but this structure could not be reproduced using the Promax rotation. Instead, seven new factors emerged. The attempt to characterise their psychopathological content clinically makes an interpretation mandatory. We formulated these factors tentatively:

(a) Psychomotor activity
(b) Social activity
(c) Structure (clear cut v. vague)
(d) Autonomous stigmatisation
(e) Drive v. lameness
(f) Intimacy v. distance-regulation
(g) Autism v. future-relatedness

The factor with the highest loading by far was Psychomotor activity. It is likely that this was partly due to neuroleptic medication, although the chlorpromazine equivalent dosages did not correlate significantly with this subscore. The seven factors reflect the psychopathological complexity of the

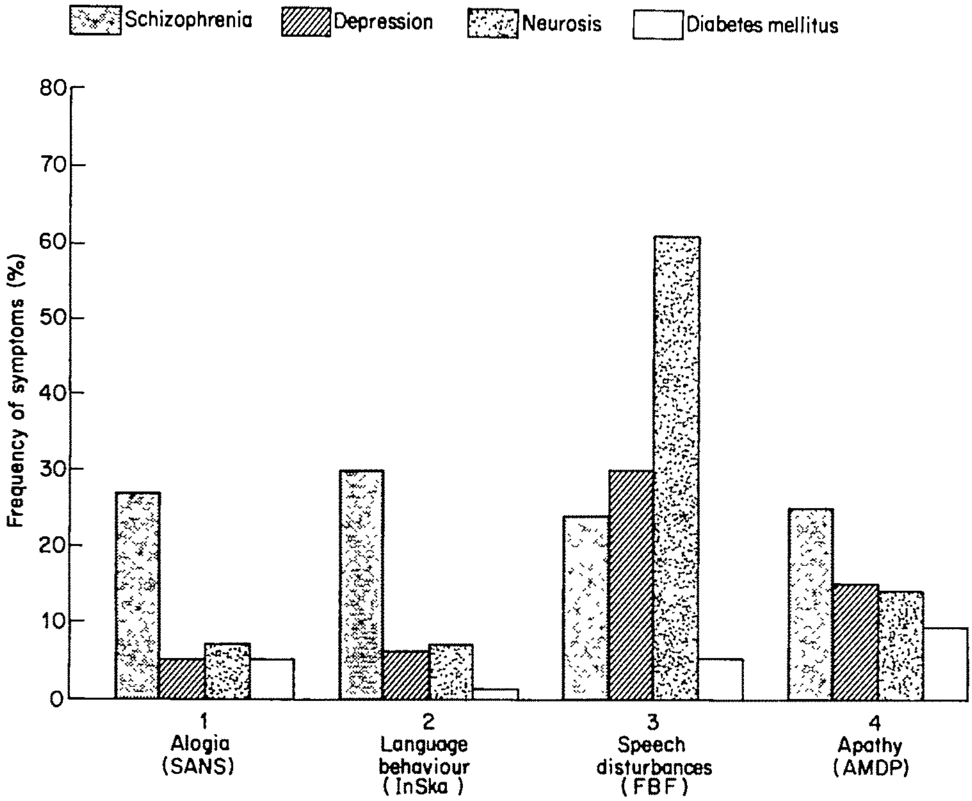

FIG. 3 Subscores language and thinking (SANS, InSka, FBF and AMDP).

syndrome. Some factors might be regarded as representing different kinds of retreat or regression from social life in so far as it is a challenge to self-assertion and intentionality; some factors, however, can be interpreted in terms of anxiety reactions including, for example, autonomous arousal or loss of psychic structure.

Discussion

The negative syndrome, as represented by the psychometric instruments SANS and InSka, appears to be a complex pattern of behaviour and emotional states. They may partly be an expression of an elementary deficiency of mental functions, partly of reactions and attitudes stemming from the whole personality, and partly they may be due to neuroleptic side-effects. This is in line with clinical experience.

Rating scales such as the SANS and the InSka must necessarily be less able to differentiate than the holistic approach taken by an experienced clinician. This, of course, refers to the reliability–validity dilemma when constructing tests. But rating scales have the advantage of being more objective than clinical impressions and thus one may be confident that the instruments are reporting something that is true when they describe at least two psychopathological strata of the negative syndrome. The first stratum is fairly specific, showing very little overlap with other diagnostic groups. It is essentially defined in terms of thinking disturbances. Loosening of associations, however, was the main primary symptom of schizophrenia for Eugen Bleuler and it is still given this status in the schizophrenic axial-syndrome of the Viennese criteria; the latter and the Bleulerian diagnostic systems for schizophrenia seem to belong to the most narrow ones. The psychopathological core of this first stratum *per se*, then, does not seem to justify stipulating either the existence of a special subgroup of negative schizophrenia nor of any new syndrome within the schizophrenic spectrum.

The second stratum also has the highest scores in schizophrenics but there is a very broad overlap with the other diagnostic groups. It covers different kinds of withdrawal behaviour as well as emotional states of apprehension, depression and resignation. These features are certainly not specific to schizophrenia, yet

TABLE I
Classificatory accuracy of subscores

Subscore	*Accuracy (%)*	*Cut-off point*	*Youden-Index*	*Sensitivity (%)*	*Specificity (%)*
SANS 2 Alogia	86	5	0.58	65	93
InSka 2 Language	86	1	0.58	55	96
InSka 4 Autism	86	1	0.48	50	98
InSka 1 Motor Activity	82	3	0.46	55	91
AMDP 5 Apathy	82	5	0.43	50	93
InSka 6 Social Activity	78	6	0.48	65	83
InSka 5 Initiative	77	5	0.40	55	85
InSka 3 Affect	75	1	0.56	85	71
SANS 1 Affect	75	3	0.40	60	80
SANS 3 Abulia	75	9	0.23	35	88
SANS 5 Attention	73	9	0.25	40	85
SANS 4 Anhedonia	70	7	0.50	85	65

TABLE II
Intercorrelations of some InSka-subscores among schizophrenics and non-schizophrenics (Spearman's r)

Schizophrenics (n=*20*) *Non-schizophrenics* (n=*60*)

Language behaviour ←→ Affective reactivity ←→ Initiative and motivation
Psychomotor activity ←→ Language behaviour ←→ Initiative and motivation
Affective reactivity ←→ Psychomotor activity ←→ Social behaviour

it does seem that schizophrenics nevertheless bear the highest risk among the groups investigated to develop the psychopathology found in this second stratum.

Further research, especially research for biological markers in schizophrenia, which needs a psychopathological grid for diagnostic subgrouping, should attempt to separate these two strata of the negative syndrome, because the nonspecific one may be linked to risk factors which are relevant across all psychiatric diagnoses as well as in healthy psychic life.

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Commentary on the Contributions of Professor H. Sass, Dr G. Gross and Dr Ch. Mundt *et al.* on 'Negative' and 'Basic' Symptoms of Schizophrenia

SIR MARTIN ROTH

These three papers by psychiatrists from the German-speaking world all deal mainly with the nature and aetiological basis of the psychological deficits manifest as 'negative' symptoms in schizophrenic illness. There is just an echo of the controversies regarding the validity of subdivision of schizophrenia into 'positive' and 'negative' forms that have received much attention from British and North American psychiatrists in recent years. (Andreasen *et al*, 1982; Crow, 1985). It appears to be implicitly assumed that schizophrenia is a unity. The acute psychoses which are diagnosed as schizophrenic in most countries but named 'psychogenic psychoses' in Scandinavia and 'bouffée delirante' in France and 'emotion psychoses' in Switzerland (Labhardt, 1963) are not allowed to complicate matters.

In his interesting historic review Dr Sass traces the concept of 'negative' or 'insufficiency' hypotheses of schizophrenia to the seminal book of Griesinger and thence to the contributions of Hughlings Jackson, Reynolds and Kraepelin. The failure to discover organic or other causes of schizophrenia should have led each generation of psychiatrists to try and define some basic deficit that could successfully subsume all the complex psychopathology, motor and behavioural disturbance, and the turmoil in the inner mental life of schizophrenic patients, within a single disturbance of psychic function. Once such a fundamental disturbance in mental life had been brought to light the discovery of the specific cerebral lesion underlying schizophrenia might, it was hoped, come within reach. Work on 'negative' symptoms and related concepts has from the outset been inspired by the belief that they were direct manifestations of cerebral lesion and that they might provide a signpost to its character and location.

The paper by Dr Gross is devoted to the teaching of the Bonn School led by Huber. She describes the primary symptoms judged in Bonn to be closer than other psychotic phenomena to the 'somatic substrate' or the cerebral origin of schizophrenia. Within the first main group are the 'direct dynamic deficiencies' which include physical and mental fatigue, diminished energy and resilience, and impaired efficiency leading to tension, insomnia, perseveration of thought, and vegetative disturbances. These and the symptoms that follow in subsequent stages of the disorder are held to arise from a genetically determined disturbance in the limbic system. In organic terms schizophrenia is therefore designated as a 'limbopathy' by the Bonn group.

Other findings of this school seemingly have implications for treatment, prevention and prognosis. Early pharmacological and psychological treatment may prevent the basic psychological deficiency from progressing beyond a threshold point into an irreversible schizophrenic psychosis. These claims appear to be open to tests by means of clinical trials.

Dr Sass reviews the deficit theories of psychiatrists such as Kraepelin and Bleuler in the early part of this century. He attaches particular importance to the contributions of Berze, who believed that 'insufficiency' and lowering of psychic activity was the primary psychological defect in schizophrenia. It blurred the distinction between the worlds of reality and the imagination, caused impairment of the will and control and gave rise to incoherence of thought. Such apparently positive features as delusions and excitement stemmed from removal of normal inhibition which arose in turn from psychic insufficiency. This primary defect was regarded by Berze as closely related causally to the underlying organic lesion in schizophrenia.

Jaspers had exerted a powerful influence on Berze. The stamp of his teaching is clearly evident in each of the three papers by German contributors. The distinctive version of 'phenomenology' expounded by Jaspers aimed at understanding subjective experiences, motives, emotions, and drives as well as the outward behaviour of the individual through the use of empathy, insight, and experience all derived in part from introspection. The patient's historical development was systematically investigated in an attempt to discover meaningful connections between the sequence of his past experience and vicissitudes and his current behaviour and inner mental life. With the aid of such forms of enquiry and examination the mental states of normal subjects and patients with neurotic and personality disorders could be understood. But the symptoms and mental lives of schizophrenic patients were beyond the reach of understanding.

In neuroses and kindred disorders, which were variants of the norm, attempts to define causal factors by application of methods of natural science were futile. In the case of schizophrenia, on the other hand, the

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patterns of conduct displayed strange and unfamiliar features '. . . not deducible from what was known of the personality, age and circumstances of life'. The same situation obtained wherever all attempts at comprehension through clinical exploration and analysis failed as they would for example in the case of early Alzheimer's disease or frontal lobe tumour. Jaspers considered that in these groups of disorders the methods of the natural sciences were appropriate. They would be likely to prove fruitful in the search for and the diagnosis of causes in the present or through the advancement of knowledge in the future.

Jaspers' concepts were of seminal importance and enriched the methods of clinical exploration and scientific enquiry for a period. But the contrast between 'developmental' disorders and 'disease process' proved too sharply drawn. The advances of the last few decades have refuted the prediction that natural sciences would prove to reveal nothing of significance regarding the origins of neuroses and personality disorder. Recent advances in relation to agoraphobic and panic disorders exemplify this point with particular clarity.

It would seem that the method of clinical exploration and analysis introduced into psychiatry by Jaspers remains influential in Germany. The rich harvest reaped here includes such elusive psychological phenomena as 'emotionality' 'drive' 'intention' and 'dynamic derailment' and 'insufficiency' among others. Few questions appear to arise about the reliability of assessment of such constructs, their independence from each other, or their validity. But Dr Mundt and his colleagues employed rating scales in their studies.

The distinguished contemporary occupant of Jaspers' Chair in Heidelberg, Professor Janzarik, has in the last 30 years arrived, through forms of exploration that stem from Jaspers, at a subdivision of schizophrenic disorders reminiscent of the Type 1–Type 2 classification. With the aid of a 'structural dynamic' analysis he has differentiated between schizophrenia in which a 'dynamic derailment' is manifest and a distinct group characterised by 'dynamic insufficiency'. The former responds favourably to neuroleptic compounds whereas the 'insufficient' groups prove refractory to all somatic therapies (Janzarik, 1987). As Dr Sass points out, this dichotomy corresponds closely to the 'positive' and 'negative' syndromes of Crow in England and Andreasen and others in the USA.

Residual negative symptoms such as apathy which may persist even after effective treatment are attributed by Janzarik to premorbid personality deficits rather than the effects of psychotic disorder. There is a close resemblance here to the views of Lewis & Murray (1987) who have concluded that such premorbid personality deficits often originate from cerebral injury sustained in the course of obstetric complications. However, Huber and his colleagues attribute 'negative symptoms' to the uninterrupted progression of the psychosis — an outcome that can be averted by appropriate and timely intervention.

All of these authors seem to regard negative symptoms with a probable origin in a cerebral lesion as an invariant and fundamental feature of schizophrenic illness. For example, in the studies with the aid of two rating scales, reported here by Dr Mundt *et al*, it was the language subscores defining the phenomenon of 'alogia' which discriminated most sharply between schizophrenic patients, on the one hand, and those with depression, neurotic disorder, and somatic disease on the other.

Problematic issues

A number of questions arise. 'Understanding' plays an indispensable part in clinical practice, entering even into the assessment of clinical features noted in the course of application of standardised forms of examination such as Wing's PSE. But it is essential to determine the reliability of the inferences drawn regarding ill-defined dimensions of mental functioning from subjective and intuitive methods. Further, when the results are incorporated into general theories about the causation of schizophrenia their validity requires exposure to stringent empirical tests if they are to be lifted from the realm of speculation. It is unclear, for example, whether the validation of Janzarik's subdivision of schizophrenia, by differences in response of his groups to somatic treatment, is based on impressions or controlled trials.

As far as the work of the Bonn School is concerned if schizophrenia can indeed be partitioned into relatively distinct groups — namely one with a favourable and the other with a bad prognosis — the unitary concept of schizophrenia will have been demolished. Unfortunately the situation appears in the absence of solid evidence to be more similar for the present, to that described by the forensic psychiatrist Patrick McGrath (personal communication). He was referring to patients of Broadmoor hospital for the criminally insane of which he was at one time Clinical Director. He said "I could discharge 50% of my patients tomorrow without endangering any of my patients or the community at large. Unfortunately I do not know which 50% I should discharge". In other words the unity of the schizophrenic syndrome is sustained for the present by the indeterminancy of the great majority of patients at the onset of the disease.

The concept of schizophrenia that seems to be implicitly held by psychiatrists who follow in the tradition of the phenomenonological explorations of Jaspers and his followers is one of unshakeable unity. Yet observations in recent years have defined psychoses with a schizophrenic clinical profile in association with temporal lobe epilepsy of long duration (Slater *et al*, 1963), cerebral tumours in the diencephalic and the limbic regions (Davison & Bagley, 1969) and within the group of psychoses associated with chronic alcoholism (Cutting, 1978) among other organic disorders.

Murray and his colleages have subdivided schizophrenia into groups determined by genetical factors on the one hand and by exogenous agents (mainly cerebral injury in early life) on the other. The non-genetic aetiology imputed to the latter, based on the assumption that lack of a family history precludes a genetic contribution, is open to question. The main point here is that the syndrome of schizophrenia is not sharply defined but fuzzy at the edges. The 'symptomatic groups' of cases associated with brain damage and drug addiction and amphetamine and LSD in particular and what is known of the clinical features and course of these disorders cannot be omitted from consideration in any theory of aetiology of schizophrenia. Comparison and contrast of those 'symptomatic' forms of disorders in which drug dependency has ceased and cerebral lesions are stationary with 'nuclear' or 'idiopathic' forms of schizophrenia could prove informative. The clinical profiles require clearer definition and relatively little work has been done on the course, treatment response and long-term outcome of symptomatic cases compared with those of the 'nuclear' group.

There are also cracks in the unitary facade of schizophrenia in other places. Traditional schools of psychiatry choose to ignore the Scandinavian concept of 'psychogenic psychosis'. Yet the general concept was accepted by Jaspers albeit on the basis of diagnostic criteria so stringent that they can hardly ever be satisfied. That version of these disorders which allocates important causal significance to life events can perhaps be left aside. But the delusional and delusional-hallucinatory psychoses of late onset are often associated with premorbid personality disorders distinct from the schizoid and schizotypal profiles common in schizophrenia of early onset. These disorders (and the genetic factors that contribute to their development) cannot be ignored as causal agents.

Some of the chronic delusional psychoses of middle life can be judged as broadly distinct in respect of clinical profile from schizophrenia. This is less true of the paraphrenic psychoses of late life (Roth, 1954; Kay & Roth, 1961). And some genetic kinship between these groups of disorders and schizophrenia proper was originally demonstrated by pupils of Kraepelin. It has been confirmed by recent genetical findings (Kay, 1959; Kay & Roth, 1961; Roth, 1987). This kinship receives further support from a large body of other evidence.

However even these psychoses are circumscribed, emotional responsiveness is well preserved, deterioration of the affective, cognitive aspects of personality and speech and intellect are almost invariably well preserved. The response to neuroleptic treatment is similar to that of schizophrenia particularly in the late life cases. But even where delusional symptoms pursue a chronic course, distinctive features of the personality and social functioning remain intact (Retterstöl, 1970; Roth, 1979). These disorders have therefore a strong claim to inclusion within the family of schizophrenic disorders. Theories of causation of schizophrenia in all its forms derived from 'negative' symptoms, and cerebral *lesions* alone are implausible.

The involvement of the temporolimbic system in the causation of schizophrenic disorder, as implied in the concept of 'limbopathy' of the Bonn School, has been confirmed by a considerable amount of radiological and neuropsychological evidence in recent years (Weinberger, 1984; Bogerts *et al*, 1985). It should perhaps be added, however, that a heavy burden of aetiological responsibility for a wide variety of psychiatric disorders is being increasingly inflicted on this cerebral region by contemporary investigations. In addition to a role in causation of schizophrenia, and involvement also in the pathophysiology of affective illness, it has been found to be the site of important lesions in Alzheimer's disease and specific deficits have been revealed by PET Scanning (Reiman, 1988) in panic and agoraphobic disorder.

Finally, it is possible that we may, in the light of recent observations, have drastically to revise our views about the nature and significance of 'negative' and 'positive' symptoms, and the distinction between them. The neuroleptic 'clozapine' which has been submitted to fresh trials in recent years (Juul Povlsen *et al*, 1985) is not only free from extrapyramidal side-effects but has been reported in recent trials to eliminate negative as well as positive symptoms, at times, in patients regressed over many years into what appeared to be states of permanent apathy, inertia and autism (Meltzer personal communication, 1989). It is for the present associated with a risk of agranulocytosis but this may prove a surmountable hazard. The study of the mode of action of this, and related compounds, might shed fresh light on the aetiological basis of schizophrenia.

With all this there is much of clinical interest in these papers and they provide a welcome relief from the monotonous fare of pre-set Chinese menus that have increasingly provided sustenance for clinicians the world over in the last decade.

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The Assessment of Negative and Positive Features in Schizophrenia

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It has become customary to classify the typical abnormalities of the mental state of schizophrenic patients into positive and negative features, with reference to behavioural excesses and deficits. Positive features are pathological by their presence and negative features represent the loss of some normal function. Positive features are generally considered to include delusions, hallucinations and positive formal thought disorder (Fish, 1962). Some studies (e.g. Johnstone *et al*, 1978) have also included incongruity of affect under this heading. Negative features include affective flattening, poverty of speech, retardation, apathy, lack of sociability. There is some evidence that the clinical correlates of positive and negative features may not be the same (Owens & Johnstone, 1980). Some workers (Andreasen & Olsen, 1982) but not others (Pogue-Geile & Harrow, 1984) have found that among schizophrenic patients positive and negative symptoms were negatively correlated. Although the nature of the relationship between positive and negative features is not entirely established and may not be simple (Wing, 1978) certain generalisations may be applied:

(a) Positive features are characteristic of earlier and negative of later phases of the illness (Pfohl & Winokur, 1982).

(b) The effects of drugs upon positive features are greater than those upon negative features. Thus neuroleptics produce more marked improvement (Johnstone *et al*, 1978; Angrist *et al*, 1980) and amphetamine more marked exacerbation (Angrist *et al*, 1980) of positive than of negative features.

(c) Positive features have been said to be relatively variable and negative features relatively stable (Ovchinnikov, 1968; Snezhnevsky, 1968).

Since the CRC Division of Psychiatry was opened in 1974 numerous studies of schizophrenic patients have been performed and I have assessed the mental states of more 1200 affected individuals often on repeated occasions. This experience has not enabled me to devise a blueprint for the satisfactory rating of the features of schizophrenia but it has certainly made me well aware of the difficulties of these assessments.

As far as positive features are considered, delusions and hallucinations are symptoms, and formal thought disorder (incoherence of speech) and incongruity of affect, signs. The symptoms are relatively easy to rate. While there are a few exceptions such as hypnagogic hallucinations and unusual subcultural beliefs, in general these phenomena do not occur in well people. They can usually be described in such a way that there is no great difficulty in making a decision about their presence and rating their severity according to the rules of the scale in use. It may be impossible to rate these symptoms in the presence of communication difficulties resulting from muteness or severe incoherence of speech and one is of course dependent upon the veracity of the patients account. Psychiatrists tend to believe that it is unusual for people to say that they have these symptoms when they do not and that a skilled interviewer would be able to detect an account which was not based upon psychotic experiences. In medico-legal circumstances such beliefs may be questioned and indeed disregarded. The possibility that a patient may be denying symptoms that he experiences is familiar to all those dealing with schizophrenia and particularly in the case of well organised paranoid patients, the most competent of psychiatrists cannot be sure whether the symptoms have really gone, whether the patient has learned to keep his delusions to himself or is unwilling to confide in one who has become incorporated into his delusional network. Scores may be shaded by additional ratings on evasiveness or histrionicity but in the end a decision has to be taken as to whether a symptom is present or not.

Difficulties in rating of speech and incongruity of affect relate to problems in defining the limits of normality. Normal people may not be deluded or hallucinated but are they coherent? Unedited tapes of the verbal production of even practised speakers do not always demonstrate a chain of well connected ideas and a decision has to be taken as to how much disconnection will be included within the normal range. This difficulty also applies to incongruity of affect as a degree of poor control of emotional response with, for example, inappropriate giggling is common in shy adolescents or unsophisticated persons in unfamiliar situations. Rules can be developed to deal with this problem but in the individual case there can be considerable room for doubt over the rating of minor degrees of this sign although where the abnormality is gross it is unmistakable. Similarly severe degrees of incoherence are obvious — the problems in rating concern lesser abnormalities where it may be necessary to allow the patient to speak freely at some length before an assessment can be made.

There are many rating scales which can be used to assess positive symptoms and these may be classified as follows:

(a) Based on general contact with the patient, e.g. Bunney & Hamburg (1963); Current Behavioural Schedule (Johnstone *et al*, 1985).
(b) Based on a non-structured interview, e.g. Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962).
(c) Based on a non-structured interview containing obligatory direct questions, e.g. Psychiatric Assessment Scale for Rating Chronic Psychotic Patients (Krawiecka *et al*, 1977).
(d) Based upon standardised interview, e.g. Present State Examination (Wing *et al*, 1974).

Ratings based upon general contact have the advantage that they are not restricted to small samples of the patients behaviour but clearly it is difficult to assess any experience in another person without obtaining his/her account of it. On the other hand one may suspect that an assessment made upon the basis of a single interview with a relative or total stranger may not provide a very accurate picture of a patient's mental content. It was in the light of this idea that we incorporated 'exhibited abnormal behaviour' which rates the nurses' view of the presence of delusions, hallucinations, incongruity of affect and incoherence of speech, in one of the schedules used in our studies of chronic psychosis (Owens & Johnstone, 1980; Johnstone *et al*, 1985). In fact we found that ratings of positive symptoms conducted by psychiatrists using the Krawiecka (Krawiecka *et al*, 1977) scale correlated closely with ratings of these symptoms based upon nursing observations of the patients (Johnstone *et al*, 1985) and this suggests that the problems may not be as great as we had feared.

The problems in rating negative features are more widespread. Items which would be included under this heading are incorporated in rating scales for schizophrenia (e.g. BPRS (Overall & Gorham, 1962); Krawiecka scale (Krawiecka *et al*, 1977)) and the many ward rating scales for long-stay patients include behaviours which are likely to be a reflection of negative features. As usually described, negative features are signs and are rated only on the basis of observations of the patient's behaviour. By definition they represent a lack of the attributes of the well in terms of interest, animation, emotional responsiveness, spontaneous speech etc. The necessity of defining the limits of normality is obvious but this is not always easy. For example many elderly people are less animated and talkative than the young and decisions need to be made about how much allowance if any should be made for age. Similarly cultural factors may be important here. Patients from a background which places a high value on stoicism and reticence could rate very differently on measures of negative symptoms from those belonging to cultures in which demonstrative behaviour is usual. There is evidence of relatively poor reliability in the rating of affective flattening (Luria & McHugh, 1974; Krawiecka *et al*, 1977; Endicott & Spitzer, 1978) but scales have been developed (Abrams & Taylor, 1978; Andreasen, 1982) which show a high degree of reliability between raters examining acutely admitted patients in single institutes.

A further problem in the rating of negative features is that they may closely resemble the phenomenology of other disorders particularly depression and the akinesia induced by neuroleptic drugs. Post-psychotic depression following schizophrenia was noted in 1920 by Mayer-Gross and has been described many times since then (McGlashan & Carpenter, 1976). Lack of interest, slowness and paucity of speech are well known features of depression and rate on assessments of that disorder (e.g. Hamilton, 1960) but would clearly also rate on assessments intended for negative schizophrenic features. The similarities between drug-induced akinesia and schizophrenic defect and depression have been well described (Rifkin *et al*, 1975). Confusion between drug-induced akinesia and negative features would be likely to cause especial difficulty when rating change in schizophrenic patients in relation to a drug trial. As in the case of positive features it is with regard to the rating of relatively minor degrees of abnormality that these difficulties mainly apply.

Because of these uncertainties about the assessment of the positive and negative symptoms in schizophrenia some test of the value of these ratings is desirable. Satisfactory testing is not easy to devise but some support for the value of our ratings would be provided if our findings were in keeping with the general characteristics of positive and negative features described above, i.e.:

(a) Positive features are charcteristic of earlier, and negative of later, features of the illness.
(b) The effects of drugs upon positive symptoms are greater than those upon negative.
(c) Positive features are relatively less stable than negative features.

In the treatment trials of acute and relatively early schizophrenia we have conducted at Northwick Park (Johnstone *et al*, 1978, 1983) 100% of the patients had positive features at the outset whereas in the survey of over 500 long-stay patients (Owens & Johnstone, 1980) one-third of the patients did not have any positive features at all. We cannot make too much of this, however, because the possession of positive features was an obligatory criterion for entry to the acute studies.

Table I
Scores of stability of mental state variables (calculated on the basis of percentage emergence/resolution relative to consistent presence)

Mental state features	*Percentage stability (rank)*
Anxiety	12 (9)
Depression	46 (5)
Retardation	42 (6)
Incongruity of affect	27 (7)
Incoherence of speech	26 (8)
Delusions	50 (4)
Hallucinations	62 (3)
Poverty of speech	68 (2)
Flattening of affect	70 (1)

In the trials of flupenthixol (Johnstone *et al*, 1978, 1983) we demonstrated significant drug v. placebo differences for positive but not negative features and thus positive features do indeed seem more drug responsive than negative although negative symptoms being initially less severe certainly had less room to improve.

In general it is not easy to separate the question of the drug responsivity of symptoms from their reversibility or stability but we have recently, using the Krawiecka scale (Krawiecka *et al*, 1977), with flattening and incongruity of affect rated separately, re-examined after 4 years the mental states of 92 patients who had been in a constant hospital environment during that time (Johnstone *et al*, 1987). Some had been constantly on neuroleptics and some had not had them at all. The fact that poverty of speech and flattening of affect were significantly more severe in patients not taking neuroleptics than in those taking such drugs indicates in this series that in rating these features we were not measuring drug-induced akinesia. The stability of the nine features rated was as shown in Table I. Thus in this blind study we found evidence that negative symptoms rated in this way are indeed more stable than positive.

In spite of the undeniable difficulties in rating negative symptoms evidence was found from the various studies at Northwick Park to show that negative and positive symptoms rated in our patients did conform to the general characteristics set out above. This indicates that the ratings do have some value but we have not considered that our negative symptom ratings were significantly sensitive to rate change. To try to overcome this problem we have attempted to derive objective correlates of negative symptoms. Using a computer program (video task) counts are made of particular responses using videotapes of standardised interviews. The responses used are: words (recognisable, non-recognisable and other vocalisations); verbal responses to questions (numbers and timing); changes in facial expression; eye contact (number and durations); smiles; inappropriate affective responses. This is a slow and tedious procedure but it is reliable giving high inter-rater reliabilities and test-retest reliabilities and it gives a wide range of scores which do significantly relate to clinical ratings in an understandable way (Table II).

Table II
Relationships between mental state assessments and video task ratings

Correlations between mental state assessments (Krawiecka Scale) and video task ratings	*Probability*
Words α Muteness	$P < 0.01$
Verbal responsiveness α Muteness	$P < 0.01$
Changes of expression α Flattening of affect	$P < 0.01$
Eye contact	NS
Inappropriate affective responses α Incongruity of affect	$P < 0.001$

It is our hope that this method will lessen the difficulties in rating change in negative symptoms and will allow us to attempt treatment trials of the schizophrenic defect state.

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The Manchester Scale

A Standardised Psychiatric Assessment for Rating Chronic Psychotic Patients

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The Manchester Scale (Krawiecka *et al*, 1977) was developed as a short, easy to administer instrument, sensitive to change, for screening patients with chronic psychosis.

It consists of eight 5-point rating scales which cover three areas of psychopathology. Positive symptoms consist of coherently expressed delusions, hallucinations, incoherence and irrelevance of speech; negative symptoms include flattened/incongruous affect, psychomotor retardation or lack of spontaneity and poverty of speech. Affective symptoms cover both anxiety and depression.

The instrument's predecessors include a simple interview described by Wing (1961) using a 5-point scale which allowed reliable classification of patients with chronic schizophrenia and the Clinical Interview Schedule (Goldberg *et al*, 1970) which used 22 5-point scales to allow a clinical diagnosis in the community.

The methodology involved initially producing videotapes of ten psychotic patients by two trained psychiatrists. Secondly, a full training interview was made with explanations and a detailed manual. Thirdly, this allowed new raters to train and compare their ratings with the other ten tapes. Hence it would be a relatively easy matter for new raters or centres to become skilled.

The scale is not intended to be used blindly; a working familiarity with the patients' notes is desirable. The first four ratings are based on the patient's replies to questions, the next four on clinical observations during the interview.

A reliability study has been performed. The two interview psychiatrists independently rated all ten tapes, three other psychiatrists trained on the example tapes and then rated the ten criterion tapes. The overall agreement between psychiatrists was established using Kendall's Coefficient of Concordance W, for the groups of five (all psychiatrists) and three (tape trained psychiatrists) raters.

Friedmans Two-Way Analysis of Variance by ranks was carried out for the groups of five and three psychiatrists. There were no differences between the psychiatrists in their mean severity ratings except on flatness of affect where one psychiatrist gave consistently lower ratings resulting in a significant difference ($P<0.01$) for both the three- and five-psychiatrist groups.

Suggested uses of the Manchester Scale include assessing large chronic populations, drug trials (when a simple side-effect rating is also available), and rehabilitation studies. It would also be suitable for multicentre population comparisons with the advantages of easy training and rapidity of use. Other developments hsve been suggested, including the incorporation of two further 5-point scales, 'Cooperation with the Social Situation of Interview' and 'Abnormal Movements' in the ratings by observation (Eve Johnstone personal communication). These have not been fully investigated yet.

Further work is at the moment being carried out at Manchester updating and clarifying the scale and videotapes using our experience of the last 10 years.

Reference

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The Manchester Scale*

Ratings

All ratings are on a 5-point scale:

0. Absent
1. Mild
2. Moderate
3. Marked
4. Severe

Ratings made by replies to questions

Depressed ☐
Anxious ☐
Coherently expressed delusions ☐
Hallucinations ☐

Ratings made by observation

Incoherence and irrelevance of speech ☐
Poverty of speech, mute ☐
Flattened affect ☐
Incongruous affect ☐
Psychomotor retardation ☐

Side-effects

(Rate as: 0. Absent; 1. Mild; 2. Marked)

Tremor ☐
Rigidity ☐
Dystonic reactions ☐
Akathisia ☐
Difficulties with vision ☐
Other (specify) .... ☐

Guide lines for the use of the five-point scales

In making these ratings the psychiatrist is expected to use his clinical judgement to make overall assessments about the patients in each particular area. For example, in making the rating for depression the rater should be expressing his own clinical assessment of the severity of depression, based on both the patient's demeanour and behaviour during the interview, and the history that the patient has given concerning depression. It should be emphasised that a morbid rating (2, 3, or 4) for depression does not imply that the principal diagnosis made will necessarily be an affective illness.

General rules for the five-point scale

0. Mild. The item is for all practical purposes absent.
1. Mild. Although there is some evidence for the item in question, it is not considered pathological.
2. Moderate. The item is present in a degree just sufficient to be regarded as pathological.
3. Marked. See individual definitions.
4. Severe. See individual definitions.

Depression

This does not only include the actual behaviour observed at interview — dejected pose, sad appearance, despondent manner — but should be a clinical rating which expresses the overall assessment of depression, and the contribution that this abnormality of affect is making to the abnormal mental state being rated. Whether there is a discrepancy between depression observed at interview and depressed mood reported as having been experienced in the past week, the rating made should be the greater of the two ratings.

0. Absent. Normal manner and behaviour at interview. No depressive phenomena elicited.
1. Mild. Although there may be some evidence of depression — occasional gloominess, lack of verve, etc. — the rater does not consider that it is pathological, or takes it to be an habitual trait not amounting to clinically significant depression.
2. Moderate. The patient is thought to be clinically depressed, but to a mild degree; *or* occasional depressed feelings which either cause significant distress or are looked upon by the patient as a significant departure from his usual self, in the past week.
3. Marked. The patient is thought to be clinically depressed, in marked degree; *or* frequent depressed feelings as described in No. 2 in the past week, or occasional extreme distress caused by depression.
4. Severe. The patient is thought to be clinically derpessed in extreme degree. Major depressive phenomena should be present; strongly held suicidal ideas, uncontrollable weeping, etc; *or* depression has caused extreme distress frequently in the past week.

Anxious

In addition to direct evidence of anxiety observed by the rater at interview, this rating should express the rater's view of the contribution which morbid anxiety is making to the mental state under consideration. (There may be some physiological signs of sympathetic over-activity, moist palms, mild tremor, blotchy patches in skin, etc.). Where anxiety is of such a degree that there is associated motor agitation, this will be rated on this key as not less than No. 3. Where there is a discrepancy between anxiety as observed at interview and anxiety expressed in the previous week the rating made should be the greater of the two ratings.

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A standardised psychiatric assessment scale for rating chronic psychotic patients. *Acta Psychiatrica Scandinavica*, 55, 299–308.

0. Absent. Normal mood at interview.
1. Mild. Such tenseness as the patient displays is thought either to be an habitual trait not amounting to pathological proportions or is thought to be a reasonable response to the interview situation.
2. Moderate. The patient is thought to display a mild degree of clinically significant anxiety or tension; *or* anxiety sufficient to cause significant distress has occurred occasionally in the past week.
3. Marked. The patient is thought to display a marked degree of clinically significant anxiety or tension. He may be apprehensive about the interview and need reassurance, but there are only minor disruptions of the interview due to anxiety. There may be associated motor agitation of mild degree; *or* anxiety sufficient to cause significant distress has occurred frequently in the past week, *or* anxiety has caused extreme distress for the individual concerned occasionally in the past week.
4. Severe. The patient is thought to display an extreme degree of clinically significant anxiety or tension. He may be unable to relax, or there may be major disruptions of the interview due to anxiety. There may be associated motor agitation of marked degree, or a fearful pre-occupation with impending events; *or* anxiety has caused extreme distress for the individual concerned frequently in the past week.

Flattened, incongruous affect

Flatness refers to an impairment in the range of available emotional responses; the patient is unable to convey the impact of events while relating his history, and cannot convey warmth or affection while speaking about those near to him.

0. Absent. Normal affect at interview.
1. Mild. The patient may be laconic, taciturn or unresponsive in discussing emotionally charged topics, but the rater considers that this is an habitual trait rather than a sign of illness.
2. Moderate. Clinically significant impairment of emotional response of mild degree. Definite lack of emotional tone discussing important topics; *or* occasional but undoubted incongruous emotional responses during the interview.
3. Marked. Clinically significant impairment of emotional response of marked degree. No warmth or affection shown. Cannot convey impact of events when giving history, no concern expressed about future; *or* frequent incongruous responses of mild degree or occasional gross incongruity.
4. Severe. Clinically significant impairment of emotional response of extreme degree: no emotional response whatever elicited; *or* gross frequent incongruity; fatuous, supercilious, giggling, etc., in such a way as to disturb interview.

Psychomotor retardation

0. Absent. Normal manner and speech during interview. Questions answered fairly promptly; air of spontaneity and changes of expression.
1. Mild. Although there may be evidence of slowness or poor spontaneity the rater considers that this is either an habitual trait or that it does not amount to clearly pathological proportions.
2. Moderate. The rater detects slowness, or lack of spontaneity at interview and attributes this to psychiatric illness: it is just clinically detectable. Delays in answering questions would merit this rating providing that the rater considers that it is part of a morbid mental state rather than an habitual trait of the patient.
3. Marked. Psychomotor retardation attributable to psychiatric illness is easily detectable at interview and is thought to make a material contribution to the abnormalities of the patient's present mental state.
4. Severe. Psychomotor retardation is present in extreme degree for the individual concerned.

Coherently expressed delusions

0. Absent. No abnormality detected at interview.
1. Mild. Eccentric beliefs and trivial misinterpretations: that bad weather is caused by nuclear tests; superstitions, religious sects, etc.
2. Moderate. Over valued ideas and ideas of reference, or undoubted misinterpretations. Special meanings.
3. Marked. Undoubted delusions or delusional perception are described as having occurred in the past month but the patient denies that he still holds the beliefs at present; *or* delusional ideas are expressed but they are not strongly held or incorrigible.
4. Severe. Undoubted delusions are present and are still held by the patient.

Hallucinations

The rater must therefore decide whether hallucinations have occurred in the *past week*; if so, whether they are true — or pseudo-hallucinations, and how frequently they have occurred.

0. Absent. No evidence of hallucinations.
1. Mild. The hallucinatory experiences reported to the rater are not definitely morbid, hypnogogic hallucinations, eidetic images and illusions.
2. Moderate. Pseudo-hallucinations of hearing and vision; hallucinations associated with insight — e.g. those following bereavement.
3. Marked. True hallucinations have been present in the past week but have occurred infrequently.
4. Severe. True hallucinations have occurred frequently in the past week.

Incoherence and irrelevance of speech

0. Absent. No evidence of thought disorder.
1. Mild. Although replies are sometimes odd the abnormalities fall short of those required for thought disorder: it is always possible to understand the connection between ideas.
2. Moderate. Occasional evidence of thought disorder elicited, but patient is otherwise coherent.
3. Marked. Frequent evidence of thought disorder but meaningful communication is possible with the

patient; *or* several episodes of incoherent speech occur.

4. Severe. Replies difficult to follow owing to lack of directing associations. Speech frequently incoherent, without a discernible thread of meaning.

Poverty of speech, mute

0. Absent. Speech normal in quantity and form.
1. Mild. Patient only speaks when spoken to; tends to give brief replies.
2. Moderate. Occasional difficulties or silences but most of interview proceeds smoothly; *or* conversation impeded by vagueness, hesitancy or brevity of replies.
3. Marked. Monosyllabic replies; often long pauses or failure to answer at all; *or* reasonable amount of speech, but answers slow and hesitant, lacking in content, or repetitions and wandering, that meaningful conversation was almost impossible.
4. Severe. Mute throughout interview, or speaks only two or three words; *or* constantly murmuring under breath.

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The Scale for the Assessment of Negative Symptoms (SANS): Conceptual and Theoretical Foundations

NANCY C. ANDREASEN

The Scale for the Assessment of Negative Symptoms (SANS) was the first instrument developed in order to provide for comprehensive assessment of negative symptoms in schizophrenia (Andreasen, 1982, 1983). It consists of five scales that evaluate five different aspects of negative symptoms: alogia, affective blunting, avolition-apathy, anhedonia-asociality, and attentional impairment. Each of these negative symptoms can be rated globally, but in addition detailed observations are made in order to achieve the global rating. It is complemented by a Scale for the Assessment of Positive Symptoms (SAPS), which permits detailed evaluation and global ratings of hallucinations, delusions, positive formal thought disorder and bizarre behaviour (Andreasen, 1984). Taken together, the two scales provide a comprehensive set of rating scales in order to measure the symptoms of schizophrenia and to assess their change over time.

Development of the SANS

The decision to develop the SANS grew out of a longstanding interest in phenomenology and many years of direct clinical experience in diagnosing and treating patients suffering from schizophrenia who were admitted to the in-patient service at The University of Iowa Psychiatric Hospital. Repeated close contact with such patients cannot help but lead to a 'Bleulerian' belief that delusions and hallucinations, although easier to define reliably, are not the most important, characteristic, or crippling symptoms of schizophrenia. Yet Bleulerian symptoms have tended to be neglected by phenomenologists and nosologists because of a belief that they were too imprecise.

An initial foray was made on the most important of the Bleulerian symptoms, thought disorder. A scale to assess thought disorder was developed using the empirical assumption that thought is usually inferred from speech, that speech can be observed directly, and that abnormalities in language, speech and communication can be defined precisely through careful attention to grammar, word choice, and links between sentences and clauses. The Scale for the Assessment of Thought, Language, and Communication (TLC) yielded highly reliable definitions, demonstrated that thought disorder was not pathognomonic of schizophrenia, and that it fell into two broad groups of subtypes. One group, negative formal thought disorder, was characterised primarily by poverty of speech and poverty of content of speech, while the other, positive formal thought disorder, was characterised by derailments, tangentiality, incoherence and distractible speech. We also observed that negative thought disorder, when present, tended to persist over time and to predict a poor prognosis. Unlike positive thought disorder, it was not common in mania. These findings were confirmed by two independent replications involving several hundred patients and controls over the course of several years (Andreasen, 1979*b*, *c*; Andreasen & Grove, 1986).

A second foray was made on another major Bleulerian symptom, affective blunting, through the development of an affect rating scale (Andreasen, 1979*a*). This study also indicated that affect could be defined reliably using an objective empirical approach, that abnormalities in affect were not specific to schizophrenia either, and yet that affective blunting in schizophrenia could be validated physiologically by measuring voice characteristics such as frequency and amplitude (Andreasen *et al*, 1981).

These studies confirmed that two major negative symptoms, negative thought disorder and affective blunting, could indeed be defined reliably and that they had a variety of important clinical correlates. Both these negative symptoms, while important, did not provide a complete coverage of the psychopathology frequently observed in patients with schizophrenia. Consequently, a scale was developed to provide a comprehensive coverage of all negative symptoms, adding avolition, anhedonia, and attentional impairment to the two already developed.

Basic assumptions

The SANS is informed by a series of basic assumptions.

First, while the concept of pathognomonic symptoms is psychologically appealing, it has no basis in reality. One simply cannot identify symptoms that occur only in schizophrenia and not in any other illness. Just as manics and psychotic depressives are likely to have delusions and hallucinations, so too depressives are likely to have some negative symptoms such as alogia or affective blunting. An attempt to define any psychopathological symptom so that it is specific to a single diagnosis is likely to lead to convoluted intellectual contortions or the wearing of blinkers. Therefore, the SANS and SAPS were both developed in order to define and describe reliably a wide range of symptoms. They could then be used to observe the frequency of these signs and symptoms in a variety of diagnostic categories or differences in change over time.

A second basic assumption is that reliability is best achieved through the use of objective observational items. For example, affective blunting is not defined by examining the patient's internal psychological state. Instead, it is assessed through observation of a series of external behaviours, such as mobility of facial expression, response to a stimulus such as being smiled at, quality of eye contact, use of expressive gestures, etc. As is discussed in more detail below, the fundamental soundness of this strategy has been confirmed through the repeated achievement of reliability in a wide range of cultural settings.

A third assumption is that rating scales must build on cross-sectional evaluation. They must be based on phenomena that one can observe clinically at a specified point in time, which may be an hour, a day, a week, or the past month. The particular cross-sectional window will depend on the specific goal or purpose of a study. Studies that attempt to build toward the development of diagnostic criteria may use a maximally large window (e.g. one month), while those attempting to observe change over time (as in treatment studies) may select a smaller window. The repeated use of rating scales over time can be used to build longitudinal definitions through repeated measurements and the observation of change. Rating scales cannot identify 'enduring' symptoms reliably during a single evaluation, and to attempt to do so retrospectively is risky. Consequently, if one wishes to identify enduring negative symptoms, one must do so empirically through prospective longitudinal assessments.

Fourth, ideally symptoms should be defined in such a way that their underlying neural mechanisms could be identified. All the various signs and symptoms of schizophrenia must ultimately reflect neural activity in the brain, and understanding the presence or absence of symptoms in terms of such neural mechanisms is one major long-term goal of phenomenological research. Since we do not yet know or understand these neural events, however, the best strategy is to maintain a comprehensive and flexible data base, and also an open mind.

Fifth, ideally rating scales should not sacrifice comprehensive coverage for simplicity, nor should they use premature foreclosure concerning the interrelationships between signs and symptoms. While it is tempting to use a scale that only involves one or two items and can be completed in two or three minutes, this is likely to be penny wise and pound foolish if one wishes to understand either the neural mechanisms or the longitudinal evolution of symptoms over time. Detailed comprehensive coverage that stays close to direct clinical data is the best strategy. While factor analytic techniques can be used to reduce data sets (and this may be useful for statistical purposes), nevertheless the basic data that are reduced statistically should be maintained intact and re-examined periodically. It could be argued, for example, that since negative symptoms tend to be highly intercorrelated, only one need be rated in order to save time. Yet factor analytic studies tend to be notoriously unstable (i.e. dependent upon the population sampled). Thus, if only one negative symptom were rated based on the reasoning that negative symptoms are highly intercorrelated, not only might one have invalid data, but one might fail to observe (for example) that avolition responds to treatment in some particular patients while affective blunting does not.

Sixth, ideally rating scales designed to assess psychopathology should be sensitive to change, since one major use is to evaluate whether various signs and symptoms respond to treatment. The identification of 'enduring' or 'core' or 'primary' symptoms is best achieved through repeated assessments, not through developing rating scales likely to be insensitive to change. Clinicians and investigators must also recognise that negative symptoms may be 'enduring' in some patients and 'changing' in others; thus the whole issue of stability and prognostic significance must be studied empirically and prospectively.

Reliability

The original components of the SANS, the TLC and the Affect Rating Scale, were subjected to careful scrutiny as to their reliability and were found to be highly reliable (Andreasen, 1979*a*, *b*, *c*). After the SANS itself was completed, similar reliability studies were done and supported the reliability of the entire scale (Andreasen, 1982).

Reliability studies at The University of Iowa were quickly followed by reliability studies in a variety of international settings. The SANS clearly fulfilled an important clinical and research need, for it has now been translated into Japanese, Spanish, Italian, French, German, Dutch, and Korean. Reliability data have been reported in studies in Japan, Spain, and Italy (Humbert *et al*, 1986; Moscarelli *et al*, 1987; Ohta *et al*, 1984). The reliability for the global ratings of the five major negative symptoms is summarised in Table I. As this table indicates, the reliability is consistently high in a variety of cultural settings. These results indicate the soundness of the basic strategy of using observational rather than subjective evaluations. Ideally, cross-national studies would now be appropriate. These have not as yet been conducted, however.

TABLE I
Reliability of negative symptoms (kappa coefficient)

Global rating	*USA*	*Japan*	*Italy*	*Spain*
Alogia	0.696	0.628	0.694	0.945
Affective flattening	0.877	0.721	0.688	0.844
Avolition apathy	0.763	0.749	0.747	0.860
Anhedonia asociality	0.731	0.725	0.728	0.769
Attentional impairment	0.749	0.788	0.659	0.892

It is, of course, well recognised that good reliability cannot usually be achieved without adequate training, even when observational items are stressed. A comprehensive set of training materials has been developed for the SANS, involving videotapes and case vignettes. These have been widely used in order to ensure that the SANS is being consistently used within the US, and additional investigators from many other countries have also received training in the SANS at Iowa. Our experience in such training indicates that high cross-national reliability is likely if such studies were to be conducted, since investigators from other cultures learn to calibrate against our standards quite rapidly.

Internal validation

Rating scales and diagnostic criteria can be validated both internally and externally. Internal validators include the evaluation of correlational relationships and cluster analytic techniques. External validators involve the capacity of a symptom scale or diagnostic criterion sets to predict some useful outcome measure, such as response to treatment, familial aggregation, outcome, or structural or chemical brain abnormalities. External validators are complex to apply and outside the range of this paper.

From the time of its development, the SANS was subjected to careful scrutiny in order to determine its internal validity (Andreasen, 1982). The evaluation of internal validity stressed the study of intercorrelations between the items used to make the global ratings and between the global ratings themselves. These assessments were done using Cronbach's alpha. Cronbach's alpha is a mean of the split half reliabilities for a group of items. The higher the alpha, the greater the internal consistency.

We have evaluated the SANS using Cronbach's alpha in two separate replication studies involving more than 150 patients suffering from schizophrenia. The results of these studies are surprisingly consistent. Further, similar studies have also been done in Spain, Italy, and Japan.

Consistently, these studies have shown that the individual items used to make the global ratings are highly intercorrelated with one another. These suggest that the individual items do tend to measure a single construct. In addition, the global ratings are also correlated with one another. While these results support the validity of the SANS, they also provide an additonal interesting application. The intercorrelations can be examined in order to identify whether any individual items are relatively weak measures of a particular negative symptom. Again, the results of these studies have been surprisingly consistent. They indicate that inappropriate affect tends to be relatively uncorrelated with other indicators of affective blunting and with negative symptoms as a whole (alpha = 0.28 and 0.30, respectively; alpha for other indicators of affective blunting ranges from 0.71 to 0.84). Blocking may also be a relatively weak measure of alogia (alpha = 0.38); this alpha could, however, be due to the relatively low frequency of blocking in our samples. This relative infrequency of blocking has been observed in most studies using the SANS.

Coefficient alpha for the five global ratings, based on our most recent study of 110 schizophrenic patients, is summarised in Table II.

TABLE II
Internal consistency of negative symptoms based on Cronbach's alpha

Symptom	*Reliability rating*
Alogia	0.628
Affective flattening	0.834
Avolition apathy	0.743
Anhedonia asociality	0.744
Attentional impairment	0.750
All global ratings	0.855

Summary: Strengths of the SANS

The SANS has a number of strengths that make it a useful rating scale for the assessment of negative symptoms. Its psychometric properties have been repeatedly and carefully evaluated, both within the centre where it was originally developed and in a number of other centres throughout the world. The results of these evaluations are remarkably consistent and indicate that the SANS is both reliable and internally cohesive. It is at present widely used in a variety of international settings and thus has become a relatively standard scale for measuring negative symptoms. It has comprehensive coverage and yet, once investigators are familiar with it, it can be completed relatively quickly and efficiently. It can be applied to a variety of time windows and can be used to map the evolution of symptoms over time and their response to treatment in clinical drug trials.

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Scale for the Assessment of Negative Symptoms (SANS)*

The Scale for the Assessment of Negative Symptoms (SANS) was developed in order to facilitate evaluation of five important symptoms frequently observed in 'core schizophrenia' (process schizophrenia, the schizophrenic defect state, negative schizophrenia). These symptoms include affective flattening, alogia (poverty of speech and thought), avolition, anhedonia, and attentional impairment.

Although researchers and clinicians have recognised the importance of these symptoms for many years, recent research has tended to minimise their usefulness because of concerns that they may be too unreliable or too subjective. Instead, recent research has tended to emphasise the importance of delusions and hallucinations. Very recently, interest in negative symptoms has re-emerged, as investigators have begun to suggest that they may be strong predictors of treatment response and long-term outcome and that they may be related to ventricular enlargement as manifested by CT scanning.

This rating scale was developed from two earlier instruments designed to rate affect and language behaviour: the Scale to Assess Thought, Language, and Communication (TLC) and the Affect Rating Scale. Both these instruments were shown to provide reliable ratings of language behaviour, and affect. For the present scale, items have been added so that it is also possible to evaluate avolition, anhedonia, and attention. Studies are at present underway to evaluate the reliability of these measures.

Investigators using the SANS will need to determine the appropriate 'time set' depending on the nature of their research. The instrument was developed with the expectation that in general investigators will choose to use a time set covering the past month, in a manner similar to the Present State Exam. Some of the measures, such as avolition and anhedonia, may describe relatively stable and enduring states that are not likely to change much over time. Nevertheless, an attempt was made to write the measures so that they could be used to describe the past month, in order that the instrument could be applicable to treatment and outcome studies and could be used as a measure of changes in clinical status. An attempt was also made to write the items so that they would be applicable to both in-patients and out-patients.

Each of the five measures (affect, alogia, avolition, anhedonia, and attention) has been defined in a systematic way. After a brief description and definition, each of the major symptoms is broken down into observable behavioural components which are rated on a six-point scale. Ideally, the rating of each of these components should be based on multiple sources of information, including direct observation by the investigator and others such as nurses, reports from the patient's family, and reports from the patient himself.

The rating of each of the behavioural components is followed by an item that describes the patient's subjective evaluation of the symptom as a whole. Rating of this item should be based solely on the patient's own self-report. In some instances, the subjective rating may bear no relationship at all to the overall severity of the symptom. For example patients with severe affective flattening may have little or no awareness of their degree of emotional blunting. Consequently, this item may be dropped if an additive summary score is used.

The last item describing each symptom is an overall global rating. This should be a true global rating, based on taking into account both the nature and the severity of the various components. In some cases, a single component that is present to a severe degree may lead to a very high global rating, even if the other components are not particularly severe. For example, severe poverty of speech may lead to a rating of 5 on alogia, since blocking tends to be relatively uncommon and poverty of content by definition cannot occur in the presence of severe poverty of speech.

Affective flattening or blunting

Affective flattening or blunting manifests itself as a characteristic impoverishment of emotional expression, reactivity, and feeling. Affective flattening can be evaluated by observation of the patient's behaviour and responsiveness during a routine interview. The rating of some items may be affected by drugs, since the Parkinsonian side-effect of phenothiazines may lead to mask-like facies and diminished associated movements. Other aspects of affect, such as responsivity or appropriateness, will not be affected, however.

1. Unchanging facial expression

The patient's face appears wooden, mechanical, frozen. It does not change expression, or changes less than normally expected, as the emotional content of discourse changes. Since phenothiazines may partially mimic this effect, the interviewer should be careful to note whether or not the patient is on medication, but should not try to 'correct' the rating accordingly.

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0. Not at all. Patient is normal or labile.
1. Questionable decrease.
2. Mild. Occasionally the patient's expression is not as full as expected.
3. Moderate. Patient's expressions are dulled overall, but not absent.
4. Marked. Patient's face has a flat 'set' look, but flickers of affect arise occasionally.
5. Severe. Patient's face looks 'wooden' and changes little, if at all throughout the interview.

2. Decreased spontaneous movements

The patient sits quietly throughout the interview and shows few or no spontaneous movements. He does not shift position, move his legs, move his hands, etc., or does so less than normally expected.

0. Not at all. Patient moves normally or is overactive.
1. Questionable decrease.
2. Mild. Some decrease in spontaneous movements.
3. Moderate. Patient moves three or four times during the interview.
4. Marked. Patient moves once or twice during the interview.
5. Severe. Patient sits immobile throughout the interview.

3. Paucity of expressive gestures

The patient does not use his body as an aid in expressing his ideas, through such means as hand gestures, sitting forward in his chair when intent on a subject, leaning back when relaxed, etc. This may occur in addition to decreased spontaneous movements.

0. Not at all. Patient uses expressive gestures normally or excessively.
1. Questionable decrease.
2. Mild. Some decrease in expressive gestures.
3. Moderate. Patient uses body as an aid in expression at least three or four times.
4. Marked. Patient uses body as an aid in expression only once or twice.
5. Severe. Patient never uses body as an aid in expression.

4. Poor eye contact

The patient avoids looking at others or using his eyes as an aid in expression. He appears to be staring into space even when he is talking.

0. Not at all. Good eye contact and expression.
1. Questionable decrease.
2. Mild. Some decrease in eye contact and eye expression.
3. Moderate. Patient's eye contact is decreased by at least half of normal.
4. Marked. Patient's eye contact is very infrequent.
5. Severe. Patient almost never looks at interviewer.

5. Affective Non-responsivity

Failure to smile or laugh when prompted may be tested by smiling or joking in a way which would usually elicit a smile from a normal individual. The examiner may also ask, "Have you forgotten how to smile?" while smiling himself.

0. Not at all.
1. Questionable decrease.
2. Mild. Slight but definite lack in responsivity.
3. Moderate. Patient occasionally seems to miss the cues to respond.
4. Marked. Patient seems to miss the cues to respond most of the time.
5. Severe. Patient essentially unresponsive, even on prompting.

6. Lack of vocal inflections

While speaking the patient fails to show normal vocal emphasis patterns. Speech has a monotonic quality, and important words are not emphasised through changes in pitch or volume. Patient also may fail to change volume with changes of subject so that he does not drop his voice when discussing private topics or raise it as he discusses things which are exciting or for which longer speech might be appropriate.

0. Not at all. Normal vocal inflections.
1. Questionable decrease.
2. Mild. Slight decrease in vocal inflections.
3. Moderate. Interviewer notices several instances of flattened vocal inflections.
4. Marked. Obvious decrease in vocal inflections.
5. Severe. Patient's speech is a continuous monotone.

7. Global rating of affective flattening

The global rating should focus on overall severity of affective flattening or blunting. Special emphasis should be given to such core features as unresponsiveness, inappropriateness, and an overall decrease in emotional intensity.

0. No flattening. Normal affect.
1. Questionable affective flattening.
2. Mild affective flattening.
3. Moderate affective flattening.
4. Marked affective flattening.
5. Severe affective flattening.

Alogia

Alogia is a general term coined to refer to the impoverished thinking and cognition that often occur in patients with schizophrenia (Greek α = no, none; logos = mind, thought). Patients with alogia have thinking processes that seem empty, turgid, or slow. Since thinking cannot be observed directly, it is inferred from the patient's speech. The two major manifestations of alogia are non-fluent empty speech (poverty of speech) and fluent empty speech (poverty of content of speech). Blocking and increased latency of response may also reflect alogia.

8. Poverty of speech

Restriction in the *amount* of spontaneous speech, so that replies to questions tend to be brief, concrete, and unelaborated. Unprompted additional information is rarely provided. Replies may be monosyllabic, and some questions may be left unanswered altogether. When confronted with this speech pattern, the interviewer may find himself frequently prompting the patient in order to encourage elaboration of replies. To elicit this finding, the examiner must allow the patient adequate time to answer and to elaborate his answer.

0. No poverty of speech. A substantial and appropriate number of replies to questions include additional information.
1. Questionable poverty of speech.
2. Mild. Occasional replies do not include elaborated information even though this is appropriate.
3. Moderate. Some replies do not include appropriately elaborated information, and some replies are monosyllabic or very brief ("Yes." "No." "Maybe." "I don't know." "Last week.").
4. Marked. Answers are rarely more than a sentence or a few words in length.
5. Severe. Patient says almost nothing and occasionally fails to answer questions.

9. Poverty of content of speech

Although replies are long enough so that speech is adequate in amount, it conveys little information. Language tends to be vague, often overabstract or overconcrete, repetitive, and stereotyped. The interviewer may recognise this finding by observing that the patient has spoken at some length but has not given adequate information to answer the question. Alternatively, the patient may provide enough information, but require many words to do so, so that a lengthy reply can be summarised in a sentence or two. Sometimes the interviewer may characterise the speech as 'empty philosophising.'

Exclusions
This finding differs from circumstantiality in that the circumstantial patient tends to provide a wealth of detail.

Example
Interviewer: "Why is it, do you think, that people believe in God?"
Patient: "Well, first of all because, he uh, he are the person that, is their personal savior. He walks with me and talks with me. And uh, the understanding that I have, um, a lot of peoples, they don't really uh know they own personal self. Because, uh, they ain't, they all, just don't know they personal self. They don't know that he uh, seemed like to me, a lot of 'em don't understand that he walks and talks with them."

0. No poverty of content of speech.
1. Questionable.
2. Mild. Occasional replies are too vague to be comprehensible or can be markedly condensed.
3. Moderate. Frequent replies which are vague or can be markedly condensed to make up at least a quarter of the interview.
4. Marked. At least half of the patient's speech is composed of vague or incomprehensible replies.
5. Severe. Nearly all the speech is vague, incomprehensible, or can be markedly condensed.

10. Blocking

Interruption of a train of speech before a thought or idea has completed. After a period of silence which may last from a few seconds to minutes, the person indicates that (s)he cannot recall what he had been saying or meant to say. Blocking should only be judged to be present either if a person voluntarily describes losing his thought or if, upon questioning by the interviewer, the person indicates that that was the reason for pausing.

0. No blocking.
1. Questionable.
2. Mild. A single instance noted during a 45 minute period.
3. Moderate. Occurs twice during 45 minutes.
4. Marked. Occurs three or four times during 45 minutes.
5. Severe. Occurs more than four times in 45 minutes.

11. Increased latency of response

The patient takes a longer time to reply to questions than is usually considered normal. He may seem 'distant' and sometimes the examiner may wonder if he has even heard the question. Prompting usually indicates that the patient is aware of the question, but has been having difficulty in formulating his thoughts in order to make an appropriate reply.

0. Not at all.
1. Questionable.
2. Mild. Occasional brief pauses before replying.
3. Moderate. Often pauses several seconds before replying.
4. Marked. Usually pauses at least 10—15 seconds before replying.
5. Severe. Long pauses prior to nearly all replies.

12. Global rating of alogia

Since the core features of alogia are poverty of speech and poverty of content of speech, the global rating should place particular emphasis on them.

0. No alogia.
1. Questionable.
2. Mild. Mild but definite impoverishment in thinking.
3. Moderate. Significant evidence for impoverished thinking.
4. Marked. Patient's thinking seems impoverished much of the time.
5. Severe. Patient's thinking seem impoverished nearly all of the time.

Avolition–Apathy

Avolition manifests itself as a characteristic lack of energy, drive, and interest. Patients are unable to mobilise themselves to initiate or persist in completing many different kinds of tasks. Unlike the diminished energy or interest of depression, the avolitional symptom complex in schizophrenia is usually not accompanied by saddened or depressed effect. The avolitional symptom complex often leads to severe social and economic impairment.

13. Grooming and hygiene

The patient displays less attention to grooming and hygiene than normal. Clothing may appear sloppy, outdated, or soiled.

Patient may bathe infrequently and not care for hair, nails, or teeth — leading to manifestations as greasy or uncombed hair, dirty hands, body odour, or unclean teeth and bad breath. Overall, the appearance is dilapidated and dishevelled. In extreme cases, the patient may even have poor toilet habits.

How often do you bathe or shower?
Do you change your clothes every day?
How often do you do laundry?

0. No evidence of poor grooming and hygiene.
1. Questionable.
2. Mild. Some slight but definite indication of inattention to appearance, i.e. messy hair or dishevelled clothes.
3. Moderate. Appearance is somewhat dishevelled, i.e. greasy hair, dirty clothes.
4. Marked. Patient's attempts to keep up grooming or hygiene are minimal.
5. Severe. Patient's clothes, body and environment are dirty and smelly.

14. Impersistence at work or school

The patient has had difficulty in seeking or maintaining employment (or schoolwork) as appropriate for his or her age and sex. If a student, he does not do homework and may even fail to attend class. Grades will tend to reflect this. If a college student, there may be a pattern of registering for courses but having to drop several or all of them before the semester is completed. If of working age, the patient may have found it difficult to work at a job because of inability to persist in completing tasks and apparent irresponsibility. He may go to work irregularly, wander away early, or complete them in a disorganised manner. He may simply sit around the house and not seek any employment or seek it only in an infrequent and desultory manner. If a housewife or a retired person, the patient may fail to complete chores, such as shopping or cleaning, or complete them in an apparently careless and half-hearted way.

Have you been having any problems at (work, school)?
Do you ever start some project and just never get around to finishing it?

0. No evidence of impersistence at work or school.
1. Questionable.
2. Mild. Slight indications of impersistence, i.e. missing a couple of days of school or work.
3. Moderate. Patient often has poor performance at work or school.
4. Marked. Patient has much difficulty maintaining even a below normal level of work or school.
5. Severe. Patient consistently fails to maintain a record at work or school.

15. Physical anergia

The patient tends to be physically inert. He may sit in a chair for hours at a time and not initiate any spontaneous activity. If encouraged to become involved in an activity, he may participate only briefly and then wander away or disengage himself and return to sitting alone. He may spend large amounts of time in some relatively mindless and physically inactive task such as watching TV or playing solitaire. His family may report that he spends most of his time at home "doing nothing except sitting around." Either at home or in an in-patient setting he may spend much of his time sitting in his room.

Are there times when you lie or sit around most of the day?
(Does this ever last longer than one day?)

0. No evidence of physical anergia.
1. Questionable.
2. Mild anergia.
3. Moderate. Patient lies in bed or sits immobile at least a quarter of normal waking hours.
4. Marked. Patient lies in bed or sits immobile at least half of normal waking hours.
5. Severe. Patient lies in bed or sits immobile for most of the day.

16. Global rating of avolition–apathy

The global rating should reflect the overall severity of the avolition symptoms, given expectational norms for the patient's age and social status of origin. In making the global rating, strong weight may be given to only one or two prominent symptoms if they are particularly striking.

0. No avolition.
1. Questionable.
2. Mild but definitely present.
3. Moderate avolition.
4. Marked avolition.
5. Severe avolition.

Anhedonia–Asociality

This symptom complex encompasses the schizophrenic patient's difficulties in experiencing interest or pleasure. It may express itself as a loss of interest in pleasurable activities, an inability to experience pleasure when participating in activities normally considered pleasurable, or a lack of involvement in social relationships of various kinds.

17. Recreational interests and activities

The patient may have few or no interests, activities, or hobbies. Although this symptom may begin insidiously or slowly, there will usually be some obvious decline from an earlier level of interest and activity. Patients with relatively milder loss of interest will engage in some activities which are passive or nondemanding, such as watching TV, or will show only occasional or sporadic interests. Patients with the most extreme loss will appear to have a complete and intractible inability to become involved in or enjoy activities. The rating in this area should take both the quality and the quantity of recreational interests into account.

Have you felt interested in the things you usually enjoy?
(Have they been as fun as usual?)
Have you been watching TV or listening to the radio?

0. No inability to enjoy recreational activities.
1. Questionable.
2. Mild inability to enjoy recreational activities.
3. Moderate. Patient often is not 'up' for recreational activities.
4. Marked. Patient has little interest in and derives only mild pleasure from recreational activities.

5. Severe. Patient has no interest in and derives no pleasure from recreational activities.

18. Sexual interest and activity

The patient may show a decrement in sexual interest and activity, as judged by what would be normal for the patient's age and marital status. Individuals who are married may manifest disinterest in sex or may engage in intercourse only at the partner's request. In extreme cases the patient may not engage in sex at all. Single patients may go for long periods of time without sexual involvement and make no effort to satisfy this drive. Whether married or single, they may report that they subjectively feel only minimal sex drive or that they take little enjoyment in sexual intercourse or in masturbatory sexual activity even when they engage in it.

Have you noticed any changes in your sex drive?

0. No inability to enjoy sexual activities.
1. Questionable decrement in sexual interest and activity.
2. Mild decrement in sexual interest and activity.
3. Moderate. Patient occasionally has noticed decreased interests in and/or enjoyment from sexual activities.
4. Marked. Patient has little interest in and/or derives little pleasure from sexual activities.
5. Severe. Patient has no interest in and/or derives no pleasure from sexual activities.

19. Ability to feel intimacy and closeness

The patient may display an inability to form close and intimate relationships of a type appropriate for his age, sex, and family status. In the case of a younger person, this area should be rated in terms of relationships with the opposite sex and with parents and siblings. In the case of an older person who is married, the relationship with spouse and with children should be evaluated, while older unmarried individuals should be judged in terms of relationships with the opposite sex and any family members who live nearby. Patients may display few or no feelings of affection to available family members. Or they may have arranged their lives so that they are completely isolated from any intimate relationships, living alone and making no effort to initiate contacts with family or members of the opposite sex.

Have you been having any problems with your (family, spouse)?
How would you feel about visiting with your (family, parents, spouse, etc.)?

0. No inability to feel intimacy and closeness.
1. Questionable inability.
2. Mild but definite inability to feel intimacy and closeness.
3. Moderate. Patient appears to enjoy family or significant others but does not appear to 'look forward' to visits.
4. Marked. Patient appears neutral toward visits from family or significant others. Brightens only mildly.
5. Severe. Patient prefers no contact with or is hostile toward family or significant others.

20. Relationships with friends and peers

Patients may also be relatively restricted in their relationships with friends and peers of either sex. They may have few or no friends, make little or no effort to develop such relationships, and choose to spend all or most of their time alone.

Have you been spending much time with friends?
Do you enjoy spending time alone, or would you rather have more friends?

0. No inability to form close friendships.
1. Questionable inability to form friendships.
2. Mild, but definite inability to form friendships.
3. Moderate. Patient able to interact, but sees friends/acquaintances only two or three times per month.
4. Marked. Patient has difficulty forming and/or keeping friendships. Sees friends/acquaintances only one to two times per month.
5. Severe. Patient has no friends and no interest in developing any social ties.

21. Global rating of anhedonia-asociality

The global rating should reflect the overall severity of anhedonia-asociality complex, taking into account the norms appropriate for the patient's age, sex, and family status.

0. No evidence of anhedonia-asociality.
1. Questionable evidence of anhedonia-asociality.
2. Mild but definite evidence of anhedonia-asociality.
3. Moderate evidence of anhedonia-asociality.
4. Marked evidence of anhedonia-asociality.
5. Severe evidence of anhedonia-asociality.

Attention

Attention is often poor in schizophrenics. The patient may have trouble focusing his attention, or he may only be able to focus sporadically and erratically. He may ignore attempts to converse with him, wander away while in the middle of an activity or task, or appear to be inattentive when engaged in formal testing or interviewing. He may or may not be aware of his difficulty in focusing his attention.

22. Social inattentiveness

While involved in social situations or activities, the patient appears inattentive. He looks away during conversations, does not pick up the topic during a discussion, or appears uninvolved or unengaged. He may abruptly terminate a discussion or a task without any apparent reason. He may seem 'spacey' or 'out of it'. He may seem to have poor concentration when playing games, reading, or watching TV.

0. No indication of inattentiveness.
1. Questionable signs of inattentiveness.
2. Mild but definite signs of inattentiveness.
3. Moderate. Patient occasionally misses what is happening in the environment.
4. Marked. Patient often misses what is happening in the environment; has trouble with reading comprehension.

5. Severe. Patient unable to follow conversation, remember what he's read, or follow TV plot.

23. Inattentiveness during Mental Status Testing

The patient may perform poorly on simple tests of intellectual functioning in spite of adequate education and intellectual ability. This should be assessed by having the patient spell WORLD backwards and by serial 7s (at least a 10th grade education) or serial 3s (at least a 6th grade education) for a series of five subtractions. A perfect score is 10.

0. No errors.
1. Questionable. (No errors, but patient performs in a halting manner or makes an error and corrects it.)
2. Mild but definite. (One error)
3. Moderate. (2 errors)
4. Marked. (3 errors)
5. Severe. (More than 3 errors)

24. Global rating of attention

This rating should assess the patient's overall ability to attend or concentrate, including both clinical appearance and performance on tasks.

0. No indications of inattentiveness.
1. Questionable.
2. Mild but definite inattentiveness.
3. Moderate inattentiveness.
4. Marked inattentiveness.
5. Severe inattentiveness.

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The Positive and Negative Syndrome Scale (PANSS): Rationale and Standardisation

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Over 75 years ago, Bleuler (1911) confronted psychiatry with the question of 'schizophrenia' or 'schizophrenias'. Today we recognise the heterogeneity of the condition, but we are still groping at efforts to clarify the different subtypes or subprocesses. Over the decades there have been various attempts to subclassify schizophrenia and tease apart the syndromes, none of which has been entirely successful. More recently, as a result of the work by Crow (1980) in England and Strauss *et al* (1974) in the USA, it has been proposed that two distinct syndromes can be discerned from the phenomenological profiles. The positive syndrome consists of productive features superadded to the mental status, such as delusions, hallucinations, and disorganised thinking. The negative syndrome represents absence of normal functions, such as deficits in the cognitive, affective, and social realms.

It has been speculated that these syndromes bear aetiological, pharmacological, and prognostic import (Andreasen, 1982). Specifically, the positive syndrome is thought to be an aspect of hyperdopaminergia, hence neuroleptic responsive, in contrast to a structural brain deficit thought to underlie the negative symptoms. Yet the studies assessing these hypotheses have yielded diverse and often conflicting results (cf. Angrist *et al*, 1980; Bishop *et al*, 1983; Rosen *et al*, 1984; Bilder *et al*, 1985). Thus, researchers still disagree on the distinctiveness of these syndromes, their relatedness to neuropathology, their different response to neuroleptics, and their stability over different phases of illness.

Research findings, of course, are no more trustworthy than the measures on which they are based. Instruments that are unreliable or lack validity can be expected to yield weak or inconsistent results (a Type II error) or, worse yet, misleading data (a Type I error). Therefore, the methods used for positive–negative assessment can be a fundamental source of error variance between studies and even within studies. Well characterised and standardised techniques are a clear prerequisite for meaningful study of these syndromes, their relationship to other features of schizophrenia, and their response to medication.

Although several positive–negative scales have recently been devised, none has undergone a thorough process of psychometric standardisation. Such a process implies provision of strict operational criteria to permit objective measurement; reliability analysis that includes internal, interrater, and longitudinal, or retest, reliabilities; and validation along the several dimensions of content, construct, criterion-related, and predictive validity (Kay *et al*, 1986*b*).

The widely used procedures for positive–negative assessment usually report only on interrater agreement as the index of reliability and on the criterion-related validity, i.e. on the relationship of the scales to similar measures. Meanwhile the longitudinal reliability, the stability, and the content and construct validity of these instruments have gone largely unexplored (Sommers, 1985). In particular, the construct validity of such scales has been problematic. A frequent criticism in assessing the negative syndrome is that no distinction is made between 'primary' negative symptoms, those which represent a genuine deficit state, and 'secondary' negative symptoms, those which might derive reciprocally from positive features (Carpenter *et al*, 1985). For example, the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982; see also Andreasen this volume) includes 'attention disorder'. This impairment may be a function of hyperarousal (Kay, 1981), a positive symptom, and in fact has been shown to correlate equivalently with both positive and negative clusters (Bilder *et al*, 1985; Cornblatt *et al*, 1985). Iager's Negative Symptom Rating Scale (Iager *et al*, 1985) likewise includes 'poor attention' and also 'disorientation', despite the relatedness of disorientation to either confusion — a positive symptom — or withdrawal — a negative symptom (Kay *et al*, 1986*b*).

More importantly, the construct validation of these scales has not taken into account the overwhelming co-variance of both positive and negative syndromes with global severity of psychopathology (Opler *et al*, 1987) or with its exacerbation during the course of illness (Rosen *et al*, 1984). This consideration is crucial since, logically, a patient who is more profoundly ill may be expected to feature greater symptoms, regardless of their nature.

A first step in achieving sound reliability and validity is provision of strict operational criteria, which allows one to objectively elicit, define, and measure symptoms. This basic framework for psychiatric assessment has been lacking in the available positive–negative scales. Even the most widely used methods do not provide specific guidelines for the psychiatric interview, which is the actual source of data. Nor do the scales offer adequately detailed definitions to decide between different levels of symptom severity, e.g. between mild

v. moderate v. moderate-severe. Other limitations in most of the reported scales include:

(a) imbalance in the number of items comprising positive and negative syndromes; this affects their comparability and creates a disparity in their potential reliabilities;
(b) inapplicability of the scales for both typological and dimensional assessment;
(c) no evidence of consistency over time nor sensitivity for monitoring drug-related changes;
(d) no composite assessment to measure the relative predominance of positive v. negative symptoms. The researcher needs to know, for instance, that findings on the negative syndrome are specific to that syndrome, and not also true for the positive syndrome, nor simply due to greater severity of illness.

To address these limitations, our group has developed the Positive and Negative Syndrome Scale (PANSS) (Kay *et al*, 1987). This 30-item, 7-point severity scale was based originally on the 18-item Brief Psychiatric Rating Scale (Overall & Gorham, 1962) and 12 items from our Psychopathology Rating Schedule (Singh & Kay, 1975). The PANSS adaptation, however, introduced strict operational criteria for conducting the clinical interview, for defining all 30 symptoms, and for rating each of seven levels of psychopathology, covering a range between absent and extreme.

The selection of items was guided by three main considerations:

(a) items must be consistent with the theoretical concept of positive and negative psychopathology;
(b) they should include symptoms that can be unambiguously classified and are considered primary rather than derivative features;
(c) to optimise content validity, they should sample from diverse realms of functioning, such as the cognitive, affective, social, and communicative.

In this way, groups of seven positive and seven negative symptoms were formed (see Appendix I), and their respective sums provide the scores for the positive and the negative syndromes.

The remaining 16 items which cannot be linked decisively to either syndrome constitute a general psychopathology scale. This scale serves as a reference point, or control measure, for interpreting the syndrome scores. Finally, the difference between positive and negative scores yields a composite scale, which expresses the extent of predominance of one syndrome over the other. This bipolar index reveals the degree of so-called 'positivity' or 'negativity' shown on balance, and it may further serve for purpose of patient classification.

All ratings are performed in consultation with the PANSS Rating Manual, which includes detailed definitions and specific criteria for all rating points.[1] An example of the item on 'Hallucinatory Behaviour' is shown in Appendix II. As a rule, the severity of a symptom is gauged according to its prominence, its extensiveness, its frequency, and above all, its disruptive impact on daily functioning. The ratings in general are based on the totality of information from the previous week. This derives both from reports by primary care staff or family and from a formalised 30–40 minute clinical interview, also described in the PANSS Rating Manual. The interview permits direct observation of affective, motor, cognitive, perceptual, attentional, integrative, and interactive functions. It may be conceptualised as involving four phases that progress systematically from non-directive to more structured and directive inquiry. The general aims and strategies for each phase are outlined in Table I.

We have undertaken to standardise the PANSS on the basis of several studies involving a total of 240 DSM–III diagnosed schizophrenics. These investigations helped to establish the scale's reliability, its stability, its drug sensitivity, and various aspects of validity, including criterion-related, content, construct, and predictive. The details of methods and results may be found in the various articles to be cited.

The distribution pattern of the four scales from the PANSS, as administered to 101 chronic schizophrenic in-patients, revealed characteristic bell-shaped curves (Kay *et al*, 1987). This indicates that the scores are distributed along normal continua and can be subjected to powerful parametric statistics. It also allows for conversion of raw scores into percentile ranks (cf. Kay *et al*, 1987), which then provides for normative tables that permit interpretation of an individual's profile in relation to the reference group.

The interrater reliability of the PANSS (see Table II) was between 0.83 and 0.87 for the four scales, with all correlational values highly significant ($P < 0.001$) (Kay, *et al*, 1988). The internal reliability of the method was examined by coefficient alpha (Kay *et al*, 1986*c*). The results indicated that each of the items within the positive and negative scales correlated strongly with the scale total. Overall the alpha coefficients were 0.73 and 0.83, respectively, and no gains could be achieved by discarding any individual items. The mean item-total correlations were 0.62 and 0.70, respectively, in contrast to nonsignificant cross-correlations of 0.17 and 0.18. The general psychopathology scale similarly

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[1] The PANSS Rating Manual is available on request from the authors.

TABLE I
Organisation of the PANSS interview

Phase	*Strategy*	*Objectives*	*Approximate time (min)*
I	Non-directive	Establish rapport Observe spontaneous behaviour Identify areas of concern	5–10
II	Semi-structured	Systematic elicitation of symptoms and their severity	15–20
III	Structured	Assess mood, anxiety, orientation, and abstract reasoning	5–10
IV	Directive	Clarify information Test limits and response to stress Assess full range of psychopathology	5–10

showed a satisfactory alpha coefficient of 0.79 as well as a split-half reliability coefficient of 0.80. All of these observed values were significant beyond $P<0.001$.

It was possible to assess test-retest reliability and stability on a cohort of chronic schizophrenics who were unresponsive to neuroleptic treatment and, therefore, remained hospitalised on our unit (Kay *et al*, 1987). Across a 3–6 month period we found no significant change in level of scores, while the longitudinal correlations were quite high: 0.80 for the positive scale and 0.68 for the negative scale.

For purpose of criterion validation, we analysed the association of the PANSS with the Andreasen (1982) method of positive–negative assessment, the SAPS and the SANS (Kay *et al*, 1988). The results (Table II) showed significant correlations between corresponding scales: $r=0.77$ for positive and $r=0.77$ for negative. Similarly, the general psychopathology scale of the PANSS correlated significantly with the Clinical Global Impressions Scale of the National Institute of Mental Health (Guy, 1976), $r=0.52$, $P<0.001$.

As a method of construct validation, we looked at the associations among our positive, negative, and general psychopathology scales (Kay *et al*, 1987). The two syndrome scales were directly related to severity of illness and also to each other (see Table II). Once their

TABLE II
Reliability and validity studies of the PANSS

	PANSS Scales			
Type of analysis	*Positive*	*Negative*	*Composite*	*General psychopathology*
Reliability analysis				
interrater (*r*)	0.83***	0.85***	0.84***	0.87***
internal (alpha)	0.73***	0.83***	—	0.79***
test-retest (*r*)	0.80***	0.68**	0.89***	0.60*
Validity analysis				
r with Andreasen or CGI	0.77*** (SAPS)	0.77*** (SANS)	—	0.52*** (CGI)
r with PANSS GPS	0.68***	0.60***	0.07	—
PANSS positive–negative intercorrelation	0.27** (simple *r*) −0.23* (*r* after partialing out GPS)			

$^{*}P<0.02$; $^{**}P<0.01$; $^{***}P<0.001$.
Based on Kay *et al* (1987, 1988). See text for explanation.
Abbreviations: PANSS: Positive and Negative Syndrome Scale; SAPS: Scale for Assessing Positive Symptoms; SANS: Scale for Assessing Negative Symptoms; CGI: Clinical Global Impressions Scale; GPS: General Psychopathology Scale.

shared variance with general psychopathology was partialled out, however, the positive and negative scales proved in fact to be *inversely* correlated ($P<0.02$). This suggests that, on face value, the two syndromes tend to co-vary, because sicker patients probably show greater manifestations of all kinds. Yet when controlling for degree of illness, positive and negative syndromes tend to be mutually exclusive, i.e. the higher the one, the lower the other. Therefore, these constructs as measured on the PANSS appear to represent discrete, non-overlapping aspects of the schizophrenic illness.

Our study of 101 chronic schizophrenics also supported the discriminant and convergent validity of the PANSS syndromal assessment in relation to independent clinical, genealogical, psychometric, and historical measures (Kay *et al*, 1986*c*). The findings from this dimensional study and a separate typological investigation of chronic schizophrenics (*infra*) are broadly summarised in Table III. The positive scale was significantly distinguished by unusual thoughts, anxiety, anger, preoccupation, disorientation, labile affect, more frequent episodes of hospitalisation in a 2½-year follow-up, and greater likelihood of sociopathy in first-degree relatives. By contrast, the negative scale was uniquely associated with slowed motor activity, deficits on affective measures, impoverished thinking, lesser education, dysfunction on cognitive developmental tests, and family history of psychosis but not affective disorders. Neither scale correlated with extraneous variables such as race, cultural group, chronicity of illness, or depressive symptoms. We concluded, accordingly, that the negative scale appears to assess a syndrome that is distinguished by familial, early developmental, and current multimodal deficits. These co-variates of the negative syndrome imply a more pernicious disease process, one devolving from genealogical and ontogenetic sources (Kay *et al*, 1985; Opler & Kay, 1985; Kay & Opler, 1987).

The criterion-related validity of the PANSS as used for typological distinction was supported in two separate studies of 37 acute and 47 chronic schizophrenics. Significant inverse relationships between positive and negative items were obtained in both studies ($r=-0.62$ and -0.55, respectively, $P<0.01$). In the acute sample (Lindenmayer *et al*, 1984), patients who were classified as negative subtype (i.e. at least three 'moderate' negative symptoms on the PANSS) differed significantly from the positive subtype in terms of lesser education, poorer work adjustment, likelihood of non-paranoid subdiagnosis, and various deficit symptoms that encompassed the cognitive, social, affective, and motor spheres. The chronic study (Opler *et al*, 1984) found the negative subtype distinguished by lesser education, likelihood of winter birth, earlier onset of illness, more primitive cognitive developmental test profile, and slower psychomotor rate, despite similar intelligence, visual-motor test scores, chronicity of illness, general psychopathology scale scores, and demographic characteristics (sex, race, cultural background). As in the dimensional study, therefore, the typological analyses supported the validity of the PANSS in relation to both antecedent and concurrent variables.

Three treatment studies provided evidence for the drug sensitivity and/or predictive validity of the PANSS. In a single-subject experimental study involving a 27-week double-blind reversal design (Kay & Opler, 1985), we

TABLE III
Distinguishing features of positive and negative syndromes in chronic schizophrenia

Area	*Positive syndrome*	*Negative syndrome*
Family history	Sociopathy (present)	Probable schizophrenia (present) Major affective illness (absent)
Pre-morbid history	Relatively unremarkable	Lesser education Cognitive developmental deficits
Course of illness and demographics	More previous hospitalisations Longer subsequent hospitalisation	Earlier onset of illness Older Winter birth Predominantly male
Clinical	Florid presentation Bizarre thinking Affective lability and anger Anxiety, preoccupation, and disorientation	Multimodal deficits Impoverished and rigid thinking Affective dulling Motor retardation

Based on Kay & Opler (1987).

compared the benefit of L-DOPA when used adjunctively with neuroleptics (Weeks 16–23) v. placebo-neuroleptic combination (Weeks 12–15 plus 24–27). Significant improvement with L-DOPA was found on the negative scale of the PANSS ($P<0.05$) as well as on two individual negative items (difficulty in abstract thinking and passive/apathetic social withdrawal). In contrast, no significant changes were achieved on the positive scale nor any of its items ($P>0.50$).

A second investigation employing a similar placebo-controlled reversal design focused on the specificity of adverse clinical responses to anti-cholinergic drugs (cogentin or trihexyphenidyl) when taken with neuroleptics (chlorpromazine or haloperidol) (Singh *et al*, 1987). The results with 47 schizophrenics indicated that only the positive scale was adversely influenced by anti-cholinergics ($P<0.02$) and that the positive and negative scales did *not* covary in their response to this intervention. Furthermore, only the patients who had been prospectively classified by the PANSS during a drug-free baseline as 'positive subtype', as defined by a composite scale score above zero, showed subsequent clinical worsening when anti-cholinergics were later introduced ($P<0.02$).

Thirdly, we assessed changes on the PANSS in ten neuroleptic–refractory schizophrenics who openly were tried on pimozide, a neuroleptic marketed in the USA for treating Gilles de al Tourette's syndrome (Feinberg *et al*, 1988). When pimozide was introduced after a 2-week baseline on a standard neuroleptic, significant symptomatic amelioration was observed on the PANSS negative scale after 4–6 weeks ($P<0.001$), while no changes were incurred on the positive scale. The results were consistent with the European literature, which suggests that pimozide targets the deficit features of schizophrenia (Falloon *et al*, 1978; Pinder *et al*, 1976), and supported the instrument's ability to reflect differential syndromal response to medications.

The predictive validity of the PANSS has been evident also from longitudinal follow-up studies of young acute schizophrenics with up to 2 years history of psychiatric illness since onset (Kay & Lindenmayer, 1987; Lindenmayer *et al*, 1986). These prospective investigations indicate that high negative scores in the early presentation seem to be of favourable consequence. At this stage a negative syndrome co-varied with lesser incidence of schizophrenia in the patient's family and greater incidence of affective psychosis. The PANSS negative scale also anticipated better adjustment on the Strauss & Carpenter (1974) Multidimensional Outcome Scale when the acute schizophrenics were followed up after 2 years (see Table IV). Some of the predictive correlations were surprisingly high, such as a Pearson r of 0.73 between baseline negative score and follow-up quantity of useful work. However, when assessed concurrently 2 years later, as patients traversed into the chronic phase, both positive and negative scores were associated with poorer functioning.

These differences according to phase of illness were corroborated by large-scale cross-sectional comparisons of acute, chronic, and long-term chronic schizophrenics, involving a sample size of 134 inpatients (Kay *et al*, 1986*a*). Our analyses, in brief summary, supported the

TABLE IV
Association of outcome measures with positive and negative syndromes assessed prospectively (baseline) and concurrently (follow-up)

	Baseline (predictive r)			*Follow-up (contemporaneous r)*		
Outcome measures on the Multidimensional Outcome Scale	*Positive score*	*Negative score*	*Positive v. negative difference*	*Positive score*	*Negative score*	*Positive v. negative difference*
Duration of non-hospitalisation	−0.13	0.53*	$P<0.10$	−0.30	−0.20	
Frequency of social contacts	0.04	0.39		−0.52*	−0.36	
Quality of social relations	0.02	0.48*	$P<0.10$	−0.67**	−0.45	
Quantity of useful work	0.26	0.73***	$P<0.05$	−0.60**	−0.56*	
Quality of useful work	−0.09	0.61**	$P<0.01$	−0.68**	−0.67**	
Absence of symptoms	−0.08	0.48*	$P<0.05$	−0.83***	−0.61**	
Ability to meet own basic needs	0.17	0.29		−0.05	−0.53*	$P<0.05$
Fullness of life	0.05	0.59**	$P<0.02$	−0.53*	−0.71***	
Overall level of functioning	0.04	0.47*	$P<0.10$	−0.69**	−0.69**	

*$P<0.05$; **$P<0.01$; ***$P<0.001$.
Based on Lindenmayer *et al* (1986).

good genealogical, phenomenological, and prognostic import of an early negative profile. Such a presentation was associated with absence of schizophrenia in the family and with clinical features characteristic of catatonic and depressed states. These correlations, however, appeared to reverse in the more chronic phases, at which points a negative syndrome carried the expected ominous implications.

In aggregate, this series of studies provided evidence of suitable psychometric properties of the PANSS for typological and dimensional assessment of distinct syndromes in schizophrenia. The scales proved to be normally distributed and internally consistent, and they demonstrated stability and high reliability when assessed by coefficient alpha, split-half method, interrater concordance, and test-retest index. The validation of the PANSS was supported in terms of construct and criterion-related validity, including its differential association with historical, genealogical, phenomenological, psychometric, pharmacological, and prospective follow-up measures.

We conclude that the principles by which the PANSS was developed, especially the operational criteria for the interview and ratings, contributed to its strength as a psychometric instrument and its promise for measuring distinct syndromes in schizophrenia. We hope that its use will reduce error variance in the study of positive and negative dimensions, enabling a clearer focus on the significance of these parameters for schizophrenia.

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Appendix I
Items represented in the positive and negative syndrome scale

Positive Syndrome Scale

P1. Delusions
P2. Conceptual disorganisation
P3. Hallucinatory behaviour
P4. Excitement
P5. Grandiosity
P6. Suspiciousness/persecution
P7. Hostility

Negative Syndrome Scale

N1. Blunted affect
N2. Emotional withdrawal
N3. Poor rapport
N4. Passive/apathetic social withdrawal
N5. Difficulty in abstract thinking
N6. Lack of spontaneity and flow of conversation
N7. Stereotyped thinking

General Psychopathology Scale

G1. Somatic concern
G2. Anxiety
G3. Guilt feelings
G4. Tension
G5. Mannerisms and posturing
G6. Depression
G7. Motor retardation
G8. Uncooperativeness
G9. Unusual thought content
G10. Disorientation
G11. Poor attention
G12. Lack of judgment and insight
G13. Disturbance of volition
G14. Poor impulse control
G15. Preoccupation
G16. Active social avoidance

Appendix II
Sample item from the PANSS

P3. Hallucinatory behaviour

Verbal report or behaviour indicating perceptions which are not generated by external stimuli. These may occur in the auditory, visual, olfactory, or somatic realms.

Basis for rating
Verbal report and physical manifestations during the course of interview as well as reports of behaviour by primary care workers or family.

1. *Absent.* Definition does not apply.
2. *Minimal.* Questionable pathology; may be at the upper extreme of normal limits.
3. *Mild.* One or two clearly formed but infrequent hallucinations, or else a number of vague abnormal perceptions which do not result in distortions of thinking or behaviour.
4. *Moderate.* Hallucinations occur frequently but not continuously, and the patient's thinking and behaviour are affected only to a minor extent.
5. *Moderate severe.* Hallucinations are frequent, may involve more than one sensory modality, and tend to distort thinking and/or disrupt behaviour. Patient may have a delusional interpretation of these experiences and respond to them emotionally and, on occasion, verbally as well.
6. *Severe.* Hallucinations are present almost continuously, causing major disruption of thinking and behaviour. Patient treats these as real perceptions, and functioning is impeded by frequent emotional and verbal responses to them.
7. *Extreme.* Patient is almost totally preoccupied with hallucinations, which virtually dominate thinking and behaviour. Hallucinations are provided a rigid delusional interpretation and provoke verbal and behavioural responses, including obedience to command hallucinations.

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PANSS Rating Criteria: Negative Scale (N)*

N1. Blunted affect

Diminished emotional responsiveness as characterised by a reduction in facial expression, modulation of feelings, and communicative gestures. Basis for rating: observation of physical manifestations of affective tone and emotional responsiveness during the course of interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Changes in facial expression and communicative gestures seem to be stilted, forced, artificial, or lacking in modulation.
4. Moderate. Reduced range of facial expression and few expressive gestures result in a dull appearance.
5. Moderate severe. Affect is generally 'flat', with only occasional changes in facial expression and a paucity of communicative gestures.
6. Severe. Marked flatness and deficiency of emotions exhibited most of the time. There may be unmodulated extreme affective discharges, such as excitement, rage, or inappropriate uncontrolled laughter.
7. Extreme. Changes in facial expression and evidence of communicative gestures are virtually absent. Patient seems constantly to show a barren or 'wooden' expression.

N2. Emotional withdrawal

Lack of interest in, involvement with, and affective commitment to life's events. Basis for rating: reports of functioning from primary care workers or family and observation of interpersonal behaviour during the course of interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Usually lacks initiative and occasionally may show deficient interest in surrounding events.
4. Moderate. Patient is generally distanced emotionally from the milieu and its challenges but, with encouragement, can be engaged.
5. Moderate severe. Patient is clearly detached emotionally from persons and events in the milieu, resisting all efforts at engagement. Patient appears distant, docile, and purposeless but can be involved in communication at least briefly and tends to personal needs, sometimes with assistance.
6. Severe. Marked deficiency of interest and emotional commitment results in limited conversation with others and frequent neglect of personal functions, for which the patient requires supervision.
7. Extreme. Patient is almost totally withdrawn, uncommunicative, and neglectful of personal needs as a result of profound lack of interest and emotional commitment.

N3. Poor rapport

Lack of interpersonal empathy, openness in conversaton, and sense of closeness, interest, or involvement with the interviewer. This is evidenced by interpersonal distancing and reduced verbal and nonverbal communication. Basis for rating: interpersonal behaviour during the course of interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Conversation is characterised by a stilted, strained, or artificial tone. It may lack emotional depth or tend to remain on an impersonal, intellectual plane.
4. Moderate. Patient typically is aloof, with interpersonal distance quite evident. Patient may answer questions mechanically, act bored, or express disinterest.
5. Moderate severe. Disinvolvement is obvious and clearly impedes the productivity of the interview. Patient may tend to avoid eye or face contact.
6. Severe. Patient is highly indifferent, with marked interpersonal distance. Answers are perfunctory, and there is little non-verbal evidence of involvement. Eye and face contact are frequently avoided.
7. Extreme. Patient is totally uninvolved with the interviewer. Patient appears to be completely indifferent and consistently avoids verbal and nonverbal interactions during the interview.

N4. Passive/apathetic social withdrawal

Diminished interest and initiative in social interactions due to passivity, apathy, anergy, or avolition. This leads to reduced interpersonal involvements and neglect of activities of daily living. Basis for rating: reports on social behaviour from primary care workers or family.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Shows occasional interest in social activities but poor initiative. Usually engages with others only when approached first by them.

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Only part of the PANSS Rating Manual is given here. The whole document is available from the authors or through *Social and Behavioral Sciences Documents*. The rating scale itself is described in Kay, S.R., Opler, L.A. & Lindenmayer, J.P. (1988) Reliability and validity of the Positive and Negative Syndrome Scale for schizophrenics. *Psychiatry Research*, 23, 99–110 and Kay, S.R., Fisbein, A. & Opler, L.A. (1987) The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, 13, 261–276.

4. Moderate. Passively goes along with most social activities but in a disinterested or mechanical way. Tends to recede into the background.
5. Moderate severe. Passively participates in only a minority of activities and shows virtually no interest or initiative. Generally spends little time with others.
6. Severe. Tends to be apathetic and isolated, participating very rarely in social activities and occasionally neglecting personal needs. Has very few spontaneous social contacts.
7. Extreme. Profoundly apathetic, socially isolated, and personally neglectful.

N5. Difficulty in abstract thinking

Impairment in the use of the abstract-symbolic mode of thinking, as evidenced by difficulty in classification, forming generalisations, and proceeding beyond concrete or egocentric thinking in problem-solving tasks. Basis for rating: responses to questions on similarities and proverb interpretaton, and use of concrete v abstract mode during the course of the interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Tends to give literal or personalised interpretations to the more difficult proverbs and may have some problems with concepts that are fairly abstract or remotely related.
4. Moderate. Often utilises a concrete mode. Has difficulty with most proverbs and some categories. Tends to be distracted by functional aspects and salient features.
5. Moderately severe. Deals primarily in a concrete mode, exhibiting difficulty with most proverbs and many categories.
6. Severe. Unable to grasp the abstract meaning of any proverbs or figurative expressions and can formulate classificatons for only the most simple of similarities. Thinking is either vacuous or locked into functional aspects, salient features, and idiosyncratic interpretations.
7. Extreme. Can use only concrete modes of thinking. Shows no comprehension of proverbs, common metaphors or similies, and simple categories. Even salient and functional attributes do not serve as a basis for classification. This rating may apply to those who cannot interact even minimally with the examiner due to marked cognitive impairment.

N6. Lack of spontaneity and flow of conversation

Reduction in the normal flow of communication associated with apathy, avolition, defensiveness, or cognitive deficit. This is manifested by diminished fluidity and productivity of the verbal-interactional process. Basis for rating: cognitive-verbal processes observed during the course of interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Conversation shows little initiative. Patient's answers tend to be brief and unembellished, requiring direct and leading questions by the interviewer.
4. Moderate. Conversation lacks free flow and appears uneven or halting. Leading questions are frequently needed to elicit adequate responses and proceed with conversation.
5. Moderate severe. Patient shows a marked lack of spontaneity and openness, replying to the interviewer's questions with only one or two brief sentences.
6. Severe. Patient's responses are limited mainly to a few words or short phrases intended to avoid or curtail communication. (e.g. 'I don't know', 'I'm not at liberty to say'.) Conversation is seriously impaired as a result, and the interview is highly unproductive.
7. Extreme. Verbal output is restricted to, at most, an occasional utterance, making conversation not possible.

N7. Stereotyped thinking

Decreased fluidity, spontaneity, and flexibility of thinking, as evidenced in rigid, repetitious, or barren thought content. Basis for rating: cognitive-verbal processes observed during the interview.

1. Absent. Definition does not apply.
2. Minimal. Questionable pathology; may be at the upper extreme of normal limits.
3. Mild. Some rigidity shown in attitudes or beliefs. Patient may refuse to consider alternative positions or have difficulty in shifting from one idea to another.
4. Moderate. Conversation revolves around a recurrent theme, resulting in difficulty in shifting to a new topic.
5. Moderate severe. Thinking is rigid and repetitious to the point that, despite the interviewer's efforts, conversation is limited to only two or three dominating topics.
6. Severe. Uncontrolled repetition of demands, statements, ideas, or questions which severely impairs conversation.
7. Extreme. Thinking, behaviour, and conversation are dominated by constant repetition of fixed ideas or limited phrases, leading to gross rigidity, inappropriateness, and restrictiveness of patient's communication.

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The WHO Psychological Impairments Rating Schedule (WHO/PIRS)

I. Introducing a New Instrument for Rating Observed Behaviour* and the Rationale of the Psychological Impairment Concept

Prepared on behalf of the collaborating investigators by
H. BIEHL, K. MAURER, A. JABLENSKY, J.E. COOPER and T. TOMOV

Based on the experience with the International Pilot Study on Schizophrenia (IPSS) (WHO 1973, 1979), the WHO Division of Mental Health and Centres in Sofia, Groningen and Mannheim, joined by expertise from Nottingham and Zurich, conceived a prospective study to assess the 'natural history' (Ciompi, 1980*a*, *b*; Watt *et al*, 1983; Biehl, 1987) of psychological impairments and social disabilities in patients with functional psychosis in different socio-cultural environments (Jablensky *et al* 1980).

This paper presents one of the principal instruments of the collaborative study, the WHO Psychological Impairments Rating Schedule (WHO/PIRS). With some modifications the instrument has also been used in other studies, both within and outside (e.g. Johnstone *et al*, 1986) the framework of the WHO Mental Health Programme, in some 15 countries and in several languages.

Underlying concepts: symptoms, signs (psychological) impairments and (social) disabilities

The distinction between reported symptoms of illness (Foulds, 1976; Palmer *et al*, 1981), observable signs (Carpenter *et al*, 1976) and impairments (Wing, 1976), and disabilities in social performance has been fundamental to the design of this WHO study. Although the boundaries between these concepts are not sharply delineated, the differentiation of three groups of phenomena has been shown to be useful in both physical rehabilitation (Wood & Badley, 1978) and social psychiatric work (Wing, 1976), and should be instrumental in an aetiological and classification research (Häfner *et al*, 1987).

The concept of (psychiatric) illness refers generally to reported mental states or experiences which are perceived as deviations from the normal state of health and can be described by more or less specific symptoms.

According to the International Classification of Impairments, Disabilities and Handicaps (ICIDH, WHO 1980), an impairment is 'any loss or abnormality of psychological, physiological or anatomical structure or function'. A particular impairment can also be a sign of an illness, but it always points to a function which is disturbed rather than to a specific nosological diagnosis. For example, cognitive deficit is clearly an impairment, but as such it is not disease-specific (cf. critical review of the impairment, disability and handicap concepts by Wiersma (1986)).

Disability is defined as 'any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being'. In the context of the WHO study, disability was defined as a loss or restriction of the capacity to perform particular social roles, normally expected of the individual in his habitual environment (De Jong *et al*, 1986). Figure 1 illustrates the postulated relationships between these concepts, where signs and impairments occupy an intermediate position between the more specific and presumably intrinsic symptoms and the rather unspecific disabilities, developing as 'consequences of disease' (WHO, 1980) under the influence of extrinsic factors.

These three different concepts lead to the following questions and assessment procedures in our longitudinal study:

> What inner experiences does the patient report? Symptoms, assessed by the PSE.
> What behaviour does the trained interviewer observe? Impairments, assessed by the PIRS after a semi-structured clinical interview.
> What are the patient's deficits in social settings? Disabilities, assessed by the DAS after an interview with a key informant.

This paper deals mainly with the assessment of observed behaviour, impairments in our nomenclature.

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* The PIRS is not reproduced in this volume, as a revised edition of it (the BOS) which is similar in both form and content is reproduced on pp. 81–88. The PIRS is available from the WHO, Geneva, and has been reproduced in incomplete form in *European Archives of Psychiatry and Neurological Sciences* (1986) **236**, 139–147.

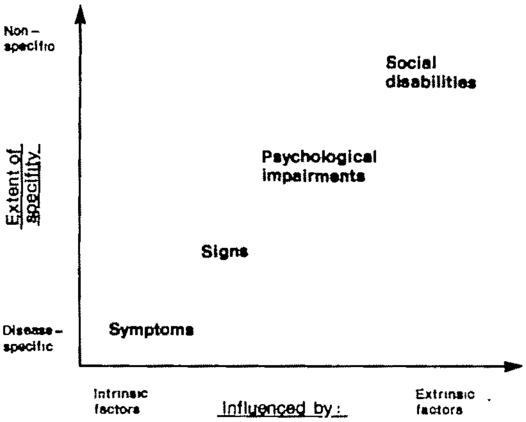

FIG. 1 Postulated relationship between symptoms, impairments and disabilities in WHO disability study.

TABLE I
Structure of the psychological impairments rating schedule (PIRS)

PIRS Sections

1. Activity/Withdrawal
   1.1 Slowness/psychic tempo
   1.2 Attention withdrawal
   1.3 Fatiguability
   1.4 Initiative (over-resp. under-)
2. Social skills
   2.1 Communication by facial expression
   2.2 Communication by body language
   2.3 Affect display
   2.4 Conversation skills
   2.5 Self-presentation
   2.6 Co-operation
3. Global impression of patient's personality (subjective)

The structure of PIRS

This instrument was designed originally to serve as a supplement to the Present State Examination (PSE) that would allow a more detailed recording of the patient's observed behaviour during the interview. Its content is an expansion and elaboration of the sections 18–20 (behaviour, affect and speech) of the ninth edition of the PSE. The concept of impairment which underlies the selection of PIRS items focusses on the interaction skills of the individual which are essential for day-to-day social behaviour and may be present and observable in most cultures. The actual selection of items was done after screening some of the literature on interactive and communicative behaviour (e.g. Ekman & Oster, 1979; Trower *et al*, 1978).

The schedule contains 97 items distributed over the 10 sections listed in Table I. A brief descriptive note is provided with each item, and a rating key allows the recording of the absence, presence, presence in a severe degree or lack of certainty about the items of behaviour. In addition, an 'overall impression' 6-point scale permits the investigator to make a more global judgment about the degree of disturbance in each of the ten sections (see full instrument in the Appendix).

How to use the PIRS

In the 10 years since it has been conceived, the PIRS has been used in a multitude of in-patient, out-patient and field settings with mental patients and former patients. Up to now, it has always been used in combination with a semi-structured clinical style interview, such as the PSE. It takes some 5 to 10 minutes extra time afterwards for the interviewer, but no additional time on part of the patient/proband is needed.

The time frame normally is the 1 hour of face-to-face contact between interviewer and patient, but some centres also experimented with extended time frames up to the 4-week period covered by the PSE. This, however, led to questions such as stability of certain behaviours/affects and to problems with retrospective reports of disturbed behaviour, not to mention issues of reliability. Therefore, we prefer a narrow time sampling approach (about 1 hour of direct interaction/interview) with most optimal time-points early in an episode (e.g. at hospital admission, even if a full PSE Interview cannot be obtained) and then again around the time of discharge into the community. Before starting to use the PIRS in research, we found — similar to experience of PSE users — an extensive training was necessary, with at least 15 video and live interviews, to achieve an adequate level of inter-rater reliability (both intra- and inter-centre).

Experience in Mannheim, where an independent series of 30 patients had been assessed in 14-day intervals during their time in hospital and at least three times after discharge yielded a kappa of 0.79 and a pairwise agreement rate of 89.4%, based on 5510 single ratings in 58 reliability interviews (out of a series of 257 interviews; see following paper).

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References to Part I and Part II are listed at the end of Part II.

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The WHO Psychological Impairments Rating Schedule (WHO/PIRS)

II. Impairments in Schizophrenics in Cross-sectional and Longitudinal Perspective — The Mannheim Experience in Two Independent Samples

H. BIEHL, K. MAURER, ELEONORE JUNG and B. KRUMM

Trimble (1986) has pointed out a shortcoming of the current wave of literature on negative symptoms: there is no overall consensus within psychiatry as to which symptoms and signs are to be considered positive and which negative (Kayton, 1973; Carpenter *et al*, 1976; Sheldrich *et al*, 1977; WHO, 1979; Andreasen, 1979; Jablensky, 1981; Crow, 1982, this volume; Rosen *et al*, 1984; Zubin, 1985; Kulhara *et al*, 1986).

It has been acknowledged that the patterns of schizophrenic psychopathology change with time, even over an extended period (Ciompi, 1980). Symptoms and signs alter during the phases of onset of the psychosis, while other changes occur both as a function of the recovery process and during the course of the illness (Pfohl & Winokur, 1982). Changes in symptoms and observed behaviour may also be conceptualised as 'occurring on a severity continuum for each discrete symptom or symptom cluster' (Carr, 1983) within a dimensional model.

One of the goals of the WHO Disability Study (Jablensky *et al*, 1980) was to show the course of symptoms of first-onset schizophrenics over 5 years, as well as the interdependence of different states of psychosis, i.e. phases with predominance of acute v phases with residual or negative symptoms and the degree to which schizophrenia leads to psychological impairments (in observed behaviour) and to severe social disabilities (deficits in role performance, Schubart *et al*, 1986*a*, *b*).

We discussed previously the course of reported symptoms in the Rhine Neckar cohort (the Mannheim part of the collaborative study; Biehl *et al*, 1986, 1988). This paper reports some of our experience with the WHO/PIRS (see Biehl *et al*, this volume) and our attempts to establish subsets of behavioural signs and impairments in analogy with the view of a natural division into 'positive' and 'negative' symptoms (Crow, 1982; Andreasen & Olsen, 1982). This study, however, was initiated in 1977/78, before this duality, which dates back to British, Swiss, and German neurologists and psychiatrists since the 1840s, had again become a main focus of attention in research (although Wing, this volume, the IPSS (WHO 1979), and work by Zubin, 1985, always continued in that tradition). Therefore, the PIRS will produce lists of positive and negative signs as a 'side-effect' of its coverage of the dimension of overt individual behaviour rather than being planned for that purpose in the first place. One note on the format of the schedule: whereas other centres developed new generations of the PIRS instrument presumably to fit better the plus/minus duality (Nottingham: BOS; see Atakan & Cooper, this volume; Groningen: CIPI, Wiersma, 1986), we in Mannheim continued to use the original instrument in several patient cohorts (up to seven cross-sections in 5 years) where it proved useful as shown below and elsewhere (Biehl *et al*, 1986), but devised more specific subscores to suit special analytic needs (POSY (positive score) and NESY (negative score) see below).

Method

Case-finding and characteristics of the Rhine Neckar cohort have been described elsewhere (Schwarz *et al*, 1980), another independent sample of 15 first-onset and 15 relapsed (first episode at least 10 years before) has been collected by one author (H. Biehl) to be assessed with the PIRS in 14-day intervals until at least 6 weeks after discharge, which produced a series of 257 PIRS Interviews, 58 of which were performed as reliability tests with a second trained rater present.

To be included in the sample, patients had to fulfill the following criteria:

(a) Residence in the defined catchment area (Mannheim, Heidelberg, and the Rhine-Neckar County, representing a total population of about 900 000).
(b) Age between 15 and 44 years at onset of symptoms.
(c) Absence of gross organic brain disease, serious mental or sensory disability, or alcohol or drug addiction.
(d) Onset of illness, defined by the criteria below, not more than 1 year before inclusion.
(e) Treatment (out- or in-patient) in one of the psychiatric hospitals serving this area (State Hospital Wiesloch, University Clinic of Heidelberg, or Central Institute for Mental Health, Mannheim).

From the view of symptoms, patients were included if suffering from:

(a) Hallucinations; and/or
(b) Delusions of non-affective type (i.e. not depressive delusions of guilt or manic delusions of grandeur); and/or

CALCUTTA
CENTRAL

(c) Thought and speech disorder (other than retardation or acceleration).

On the basis of our screening criteria, 70 schizophrenic patients with a first-onset of illness were included in the study. The 1-year incidence for the catchment area of schizophrenia, between the ages of 15 and 44 years, was 10.2 per 100 000 population (Schwarz *et al*, 1980; Biehl *et al*, 1986).

Symptoms, signs, impairments and disability were assessed at seven different time-points during the 5-year period. Three patients committed suicide within the first 3 years after initial examination. It was possible for all surviving patients to be located and contacted, 62 participated in all seven interviews.

Of the 70 subjects 41 (58.6%) were men. The mean age of the entire cohort at onset was 25 years: 34 patients (48.6%) were between 15 and 24 years old, while 10 (14.3%) were between 35 and 44 years. Fifty-two (74.3%) patients were unmarried, 12 (17.1%) married, two (2.9%) lived with a heterosexual partner, and four (5.7%) were divorced. Twenty-two patients (31.4%) lived alone, 30 (42.9%) with their parents, 14 (20.0%) with a spouse or heterosexual partner, and four in a hostel or half-way house.

Reliability

In rating symptoms, signs and observed behaviour, extensive training is necessary before starting a study. This may sound trivial, but is quite often disregarded even in the age of operationalised scales and schedules. Also, the use of indices of reliability is quite variable, as reviewed by Anker (1983), who suggested using at least two different coefficients simultaneously in order to avoid drawbacks and flaws inherent in all available methods to date.

PSE behavioural items (on which part of the PIRS is based) had earlier been found more problematic than symptoms (Wing *et al*, 1974), but in a recent study (Mignolli *et al*, 1988) using well-trained interviewers mean kappa values of 0.95 are given for the PSE behaviour sections. Whereas some centres, using up to 14 different raters with only a brief training and few patients reported lower reliability figures with the PIRS as opposed to the PSE (Slooff, unpublished), we calculated a kappa of 0.79 and a pairwise agreement rate of 89.4% on the basis of 58 interviews (after an initial training of at least 15 video and live PSE and PIRS interviews beforehand). There was some minor variation in reliability and stability, depending on 'chronic' v. 'first episode', and 'in-patient' v. 'out-patient' status (see Table I).

Stability

An important issue in discussing so-called negative symptoms is whether they are (especially) persistent or whether multiple assessments reveal an optimal time-point to identify them (Pogue-Geile & Harrow, 1984, 1985, this volume). With observed behaviour, rated on a time sampling basis (1h observation as opposed to 4 weeks as basis for PSE and DAS/WHO ratings), there is always the question of stability or fluctuation of specific behaviours/items (Bunney & Hamburg, 1963). In our satellite cohort, we calculated an overall kappa of 0.66 and a pairwise agreement rate of 82.9 for stability in 14-day intervals. On the basis of transition

TABLE I
Reliability and 14-day stability of PIRS ratings
(PIRS complete instrument: Reliability and Stability in subgroups split up for comparison)

	Acute new in-patients (*n* = *16*)	*Same group outside* (*n* = *13*)	*In-patients 'chronic'* (*n* = *16*)	*Out-patients 'chronic'* (*n* = *13*)	*All patients' reliability interviews* (*n* = *58*)
KAPPA	0.70	0.78	0.82	0.80	0.79
Reliability					
P	84.5	90.3	90.7	90.1	89.4
P_{zero}	62.3	70.6	64.9	66.5	65.9
KAPPA	0.51*	0.80	0.70*	0.68*	0.66
'Stability'					
P	73.7	91.1	84.7	84.0	82.9
$P_{zero}^{(14d)}$	58.0	70.6	63.3	60.5	63.5

* Groups with Delta (Δ) kappa ≥ 0.12 (i.e. 'prone to change').
P_{zero} ≙ proportions of concordant 'absent' ratings.
P ≙ pairwise agreement rate.

probabilities, a method for calculating a more plausible measure or stability coefficient was developed (Biehl & Krumm, 1981). The most stable single item (not unexpectedly) is affective blunting (see Table II).

Frequencies

Classical behaviour items associated with psychosis such as stereotypes, catatonic behavour, incoherence of speech, stupour, etc. were found to be quite rare and short-lasting (low stability coefficients), both in the 5-year and the brief interval repetition cohorts.

Tables III, IV and V illustrate the relative frequencies of the ten most frequent items over 5 years (where those items commonly associated with negative or minus behaviour predominate, with the exception of observed anxiety), the most frequent items, and the most rare (but still important) items in the short-term satellite study. The latter lists also give indicators of reliability per item and different coefficients of 14-day stability.

Profiles

The overall impression ratings of each PIRS section can be plotted in order to produce individual or group profiles. Figure 1 illustrates the PIRS profiles of the 70 patients at three different time-points (Q1: initial, Q4: 1.5 year follow-up, Q7: 5-year follow-up). Despite

TABLE II

PIRS: A method for calculating a stability-coefficient

Example: Most stable item in the PIRS
No 47 'blunted affect'
n = 173 transition comparisons (before/after)

0 ≙ absent
1 ≙ present

t_{j+1}
(14 days later)

		0	1
t_j(before)	0	36	14
	1	15	108

ZEILENMATRIX (line matrix of transition probabilities from t_i to t_{i+1})

	0	1
0	0.72	0.28
1	0.12	0.88

$\text{stb}_{14} = 0.88$

GESAMTMATRIX (overall matrix of probabilities)

	0	1
0	0.21	0.08
1	0.09	0.62

$\text{sta}_{14} = 0.83$

NB: stb = stable occurrence, sta = overall stability of rating/judgment.
Longer time intervals: $\text{stb}_{28\text{days}} = 0.8$; $\text{sta}_{28\text{days}} = 0.72$.
$\text{stb}_{42\text{days}} = 0.8$; $\text{sta}_{42\text{days}} = 0.7$.

TABLE III
The ten most frequent psychological impairments in schizophrenics
(single items of the PIRS, mean values over all cross-sections)

		(%)
1.	Affective blunting	34.2
2.	Efforts to control display of affect	31.6
3.	Slowness and underactivity	31.8
4.	Lack of humour	28.2
5.	Reduced quantity of expressive movements	27.7
6.	Lack of 'presence'	27.2
7.	Slowness of facial movements	26.8
8.	Observed anxiety	26.8
9.	Abnormally unmodulated voice	26.7
10.	Reduced range of facial emotions	25.5

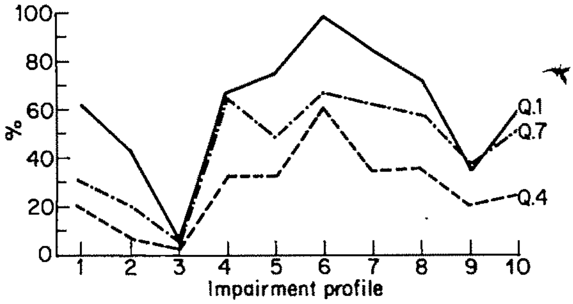

FIG. 1 Impairment profile. PIRS sections (overall impressions): 1 slowness, 2 attention, 3 fatiguability, 4 facial expression, 5 body language, 6 affect display, 7 conversation skills, 8 self presentation, 9 cooperation, 10 initiative.

considerable variation in height with highest rates of disturbance found in the sections 'Affect Display', 'Conversation Skills' and 'Body Language' at all time-points, the shapes of the curves show some similarity and could be distinguished well from those of a non-schizophrenic group we studied for pilot purposes. Still, these profiles which are also of use in social skills training (Trower *et al*, 1978; Schubart *et al*, 1986*a*), have the disadvantage of not being sensitive to the positive/overactive v. negative/apathetic polarity in observed behaviour.

Behavioural items that were commonly associated with an increase of observable activity, movements, facial emotional expression, speech, etc. were grouped

TABLE IV
PIRS: Most frequent single items (out of 75) (n = 257 interviews)

Rank	*Item*	*Positive ratings (%)*	*Reliability*		*'Stability' (14d)*		
			kappa	*P*	*kappa*	*P*	*sta*
1.	Under-use of 'non-verbal grammar'	53	0.7	79	0.4	65	0.58
2.	Blunted affect	52	0.9	94	0.7	84	0.83
3.	Limited use of gesture	51	0.8	87	0.6	77	0.80
4.	Reduction of facial movements	50	0.94	96	0.6	77	0.81
5.	Slowness	49	0.85	91	0.7	81	0.82
6.	Reduced quantity of expressive movements	48	0.8	91	0.6	75	0.81
7.	Reduced range of facial expression	45	0.8	87	0.6	77	0.76
. . . .							
12.	Perplexity	37	0.7	87	0.5	75	0.67
.							
14.	Depression	35	0.8	93	0.4	72	0.67
. . .							
18.	Anxiety	30	0.8	91	0.6	82	0.77

TABLE V
PIRS: Most rare single items (out of 75) n = 75 interviews

Rank	*Item*	*Positive ratings (%)*	*'Stability' (14 days)* *kappa*	*sta*
75.	Neologism	0.4	0.0	0.0
74.	Muteness	0.8	0.0	0.0
.		.	.	.
.		.	.	.
71.	Non-social speech	1.9	0.0	0.67
70.	Stupor	2.7	0.0	0.05
69.	Embarrassing behaviour	2.7	0.0	0.09
66.	Mannerisms	3.1	0.1	0.05
66.	Stuttering	3.1	0.0	0.14
66.	Bizarre appearance	3.1	0.0	0.06
63.	Flight of ideas	3.5	0.8	0.40
63.	Perseveration	3.5	0.5	0.09
.				
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.				
59.	Catatonic behaviour	4.7	0.3	0.16
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49.	Stereotypies	9.1	0.8	0.47

to form a POSY score (sometimes, though not necessarily associated with a psychotic episode or impending relapse, i.e. with an increase of positive/productive symptoms). Similarly, elements or signs of decrease in observable activity, tempo, initiative, gesture, etc. were combined to form a NESY score. The latter are often associated with chronic schizophrenia or residual syndromes in the interval between more active episodes, but our experience clearly showed that a high level of negative signs is already present early during the psychotic illness (Biehl *et al*, 1986, 1987).

Figure 2 shows the course of POSY (Table VI), NESY (Table VII), and an overall PIRS total score over 5 years, where POSY remains on the plateau level reached after 1.5 years, whereas NESY values increase again with time, also strongly influencing the overall score.

Most interesting, but not fully analysed (danger of age bias), are sex differences in the course of our impairment scores, with females faring obviously better than males over the first years, but with the difference being minimised after 5 years (see Häfner *et al*, 1987, fig. 10, p. 69).

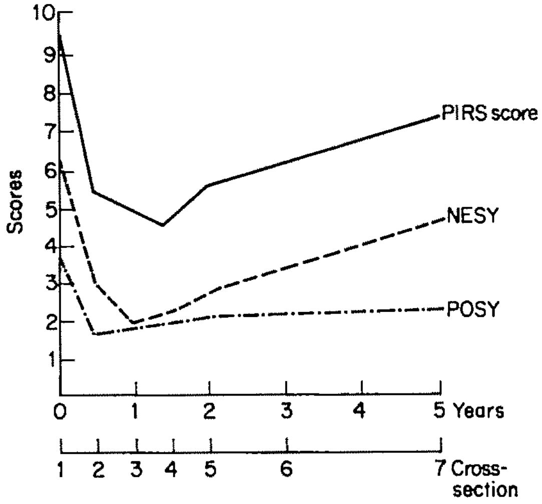

FIG. 2 Course of positive, negative and overall impairment scores over 5 years (n = 70; mean values). PIRS-Score = sum-score of impairments; NESY = sum-score of selected negative impairments (observed); POSY = sum-score of selected positive impairments (observed).

TABLE VI
POSY: Impairment items, which constitute the positive score

Item number	*Item label*
004	Stupor
006	Distractability
007	Hallucinatory behaviour
008	Blank spells
018	Over-initiative
021	Increased facial expressions
023	Inappropriateness
036	Agitation
038	Catatonic movements
042	Observed anxiety
043	Observed depression
044	Hypomanic affect
045	Hostile irritability
048	Incongruity of affect
049	Gross excitement and violence
050	Liability of mood
053	Abnormal loud voice
057	Incoherence
058	Neologisms, idiosyncrasies
060	Talking out of turn
063	Pressure of speech
066	Flight of ideas
068	Perseveration
074	Embarrassing behaviour
076	Disturbed reasoning
077	Bizarre appearance
078	Irreverent behaviour
079	Histrionic behaviour
082	Suspiciousness
083	Hostility

TABLE VII
NESY: Impairment items which constitute the negative score

001	Slowness and underactivity
002	Slow facial expression
003	Slow speech
019	Loss of initiative
020	Reduced quantity of facial expressions
022	Reduced range of facial expressions
025	Gaze avoidance
029	Facial mannerisms and stereotypies
035	Limited use of gesture
037	Bizarre posturing
039	Stereotypies
047	Blunted affect
055	Flat voice
061	Lack of 'non-verbal grammar'
062	Restricted quantity of speech
067	Poverty of content
069	Lack of humour
070	Lack of listener feedback
080	Lack of 'presence'
085	Overcompliance

Validity

The PIRS as an instrument and the *a priori* formed subscores have been tested in several ways in our centre and in Geneva. First, independent experts with clinical experience have replicated our division into PIRS sections and the *a priori* plus/minus lists; there were also minor problems with the overlap of (post-psychotic) depression and residual/negative signs. Second, we successfully tested PIRS subscores as predictors of short and long-term course and outcome (Biehl *et al*, 1986). Then, the WHO performed a principal components analysis with the PIRS data of 513 first-onset schizophrenics (using all items with more than 10% positive/present ratings) collected by the seven centres and identified a 13-item factor 1 'psychomotor inhibition' and a 2-item factor 3 'non-assertiveness' (all items of these belong to our NESY list). POSY items were found in factor 2 'agitation' (all six items), factor 4 'mood disorder' (all three items), factor 5 'parathymia' (three out of four), and factor 6 'hallucinatory behaviour' (five out of six). Finally, the POSY and NESY impairment scores showed high correlations with factor-analytically derived reported positive/productive and negative/depressive symptom (PSE Sections 1–17) scores of our Mannheim cohort over 5 years (Biehl, 1987). These and other measures of construct and content validity already calculated will be published in the near future.

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Behavioural Observation Schedule (BOS), PIRS 2nd edition

A revised edition of the PIRS (WHO, Geneva, March 1978)

Revised by Z. ATAKAN and J.E. COOPER*

The Psychological Impairments Rating Schedule (PIRS) was originally designed by the WHO (Jablensky, 1978; see also Biehl *et al* this volume) and was used as a supplement to the Present State Examination (PSE) (Wing *et al*, 1974) in a number of collaborative WHO studies. It was mainly designed for assessing selected areas of psychological and behavioural impairments (or deficits) in patients who have suffered, or are suffering, from functional psychotic disorders. It comprised items and scales for rating observed behaviour and was filled in immediately or soon after a psychiatric or PSE interview. Raters were encouraged to take note of a subject's current behaviour and function both before and after the interview proper. The first two sections of PIRS included all behavioural items of PSE (ninth edition). Sections 18–20 as well as a number of items taken from other psychopathological rating scales and items formulated *de novo*.

Early experience with the PIRS highlighted a number of problems. Most of the research centres involved (Ankara, Turkey; Gröningen, Holland; Manheim, West Germany and Nottingham, UK) had listed the 'problem items' and made remarks on various aspects of the schedule. First, there was a need for more precise definitions and rating instructions, regarding most of the items. Second, some items were found to overlap with the others. For instance, there were two items regarding gaze; 'gaze avoidance' and 'avoidance of looking' and they were basically thought to be describing the same behaviour. Third, the PIRS omitted a number of commonly observed aspects of behaviour. For example, there were no items on 'increased psychic tempo' and the section on 'initiative' needed to have more items in order to cover both lack and excess of initiative. Finally, the general organisation of the schedule needed attention to bring it more in line with the familiar order of an everyday clinical mental state examination.

The process of revising the PIRS consisted of gathering our own thoughts and also the remarks obtained from each above mentioned centre. Videotaped PSE interviews used in the reliability study for PIRS were examined and remarks made for each individual patient's behaviour and their related ratings were compared. Additional behaviours were noted and appropriate scale items were developed.

General principles of the schedule

General principles of the new version were outlined as follows:

(a) The Behavioural Observation Schedule (BOS) includes most behaviours which can be observed in a wide range of psychiatric conditions and not just those which may be seen in functional psychotic disorders. It is also intended to include items which will capture the area of threshold ratings between normal and abnormal.

(b) It should be used to supplement the PSE or other structured or semi-structured psychiatric interviews in order to obtain ratings on a wide range of observed behaviours.

(c) The order of both items within sections and sections within the schedule follows the principle of moving from the simple towards the more complicated. It is now designed such that the general order approximates to the behavioural aspects of an everyday mental state examination.

(d) Most sections have three divisions rather than two as previously. In the first division, there are a selection of individual items which can be rated on the basis of direct observation, without the rater having to make an interpretation of what he/she has observed. The second division contains another set of items which can be rated to some extent as an interpretation of observed behaviour and these are more complex in nature. The rater is therefore reminded that he/she is making an interpretation when, for instance, rating items such as 'perplexity', 'inappropriateness' or 'bizarre appearance'. The third division, within each section, deals with the rater's global impressions of the subject's functioning especially in the relevant cultural environment, i.e. how he/she would compare with an average healthy person's display of behaviour and what kind of impression would the subject leave on others.

(e) The ratings of the first two divisions described above are made on a categorical scale and each item has, as far as possible, the same pattern and the same meaning with 0 coded for absence and

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* Revised Nottingham, June 1982.

1 and 2 for increasing severity. Further guidance is additionally given in individual items when necessary. For the third division of the sections (global impressions), the ratings are made on a 6-point linear scale for which three anchor points are provided. These points contain brief descriptions of 'no disturbances', 'minimum disturbance' and 'maximum disturbance' and provide guidelines rather than strict definitions. When in doubt, or in difficulty in deciding between two neighbouring steps, the rater is instructed to select the numerically lower step, as a general rule.

(f) A new section has been added to the end of the schedule where the interviewer notes the presumed cause of the abnormalities already rated in the schedule. The causes are rated as one or more of the following: (these should all be specified)

due to drug effects
due to physical illness
due to personality traits
due to neurosis
due to functional psychosis
due to organic psychiatric conditions
no known cause.

The rater is additionally asked to specify the particular items affected.

(g) The new schedule contains an increased amount of information and examples for further guidance and the user is frequently reminded to take the subject's cultural background into account during the ratings.

Contents of the schedule

BOS consists of five main sections. The order of these is as follows:

Self-presentation

The most striking characteristics of the subject in general appearance and gait are considered here. Some other items deal with the subject's skills in presenting a favourable façade and also the degree of conforming to social routines and conventions. Most items of this section only require direct observation.

Activity

This section consists of four subsections as follows:

Sleepiness

The manifestations of sleepiness should be out of proportion to the length of the interview, or to the demands put to the subject during the examination, and should be unusual for the time of the day. Here the drop of alertness is considered to be related to fatiguability.

Attention disorders

The subject's ability to maintain and appropriately shift the focus of attention in relation to the topics discussed are considered under this subsection. Attention deficits may be due to lack of concentration or to withdrawal of attention in relation to being pre-occupied with internal experiences such as depression or hallucinations. These behaviours are separately considered.

Psychic tempo

This section is further divided into two parts; decreased and increased psychic tempos:

In *decreased psychic tempo*, the reduction of voluntary movements, slow speech and overall impression of the speed of the mental processes of the subject are evaluated.

The second part, *increased psychic tempo* deals with the increased speed of voluntary movements and a rapid, copious speech. The item on speech is only concerned with the speed of speech rather than the speed of ideas, as the latter is dealt with elsewhere in the schedule.

Initiative

This section is again divided into two parts; abnormal lack of initiative and abnormal excess of initiative:

In the first part, *abnormal lack of initiative* is considered. Although it is likely that during the interview, the subject may not have the opportunity to manifest the whole potential of initiative, there can be occasions for the subject to display various forms of initiative when the interviewer first meets the subject and also during parting after the completion of the interview. Some subjects can loose initiative because of their neurotic symptoms and pre-occupation with their problems, while some others lose theirs with psychotic symptoms. Both these types of lack of initiative are included here.

In the second part, *abnormal excess of initiative* is evaluated. The subject may be expressing his/her personal opinions or making too many requests or demands; both being more than it is naturally expected or appropriate during an interview situation.

Display of affect

This section consists of three subsections as follows:

Display of quantity of affect

This section is involved with the ratings of quantity of emotions and rate of changes, irrespective of the individual emotion shown, which is dealt with in the next section. Some subjects may display a reduced quantity and/or range of expressive facial and bodily movements, while others can have an increased quantity, or show gross excitement or lability of mood.

Display of quality of affect

This section is involved with the nature and quality of emotions.

The ratings are made on the observed manifestations of affect and mood such as anxiety, depression or irritability.

Other disturbances of facial expression

This section is involved with some other characteristics of facial expression which are not a matter of quantity alone and may be more complicated in nature. For instance, the subject may display rather unusual facial expressions such as facial mannerisms or stereotypies or have gaze avoidance and abnormal stare which are well beyond the culturally accepted norms.

Communication skills

This section has two subsections as follows:

Communication by 'body language'

The subject's posture and gestures indicating openness for communication or distance are considered here. The amount and range of expressive gestures, presence or absence of idiosyncratic body movements such as stereotypies or mannerisms are rated. Items regarding varying types of withdrawn postures or restlessness are also dealt with under this section.

Verbal communication-conversation

This section is divided into three parts.

The first part deals with the *decreased elements of conversation*. Here the reduced elements in the quality of voice and delivery, the amount and flow of speech, poverty of content of speech and lack of conversational skills are considered. Overall ratings are made according with the subject's ability in engaging in a conversation.

The second part involves *increased elements of conversation*. Here the relevant characteristics such as having an abnormally loud voice or abnormally lengthy and circumstantial speech or making jokes at inappropriate occasions are rated. Overall ratings are made whether or not the subject would make a disturbed effect on others in a normal social situation.

The third part includes *other elements of conversation* and deals with the quality and the flow of speech and the appropriateness of the interaction with the interviewer in conversation. Some items such as stuttering, disturbance of articulation or persevaration can be seen in organic disturbances. Other items concentrate on the grammar and the logical links used by the subject, as in incoherence. Neologisms and idiosyncratic use of words are also considered here. The user is asked to write down the examples of these rather rare items in order to ensure that they could be checked afterwards for correction.

Co-operation

The mutual relations of the subject with the interviewer (and presumably with the other people) and additionally the degree of his/her co-operation are examined in this section. The subject may look suspicious but may or may not be overtly suspicious of the interview procedure or of the interviewer. Hostility can again be overt or subtle and the subject may be giving misleading answers, all these aspects concerning these descriptions are covered in this section. On the other hand, there may be verbal overcompliance when the subject is passively submissive or he/she is mainly trying to please the interviewer. The global ratings are made according to the degree of willingness shown to co-operate with the interviewer and the interview.

The use of the BOS

The schedule has been recognised by the WHO but has not yet been translated into other languages. It has so far been used in a local study and a good reliability was achieved between the two raters (Z. Atakan and T. Craig). This study involved watching 20 videotaped PSE interviews (conducted by one of the raters) and making ratings at the same time. It took approximately 15 minutes to complete the ratings for each patient and had a good face validity. The schedule will be used in two other studies, which are going to take place in the University of Nottingham and Guy's Hospital, London. What is required at this stage is a wider scale reliability study, as this would especially deal with the problem of testing reliability for the rare items.

Although the new version contains an increased amount of information, there is still a need to provide a 'user's manual' and further work is in progress to guide the rater.

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Behavioural Observation Schedule (BOS)*

1. Self-presentation

Consider:
(i) the most striking characteristics of the subject in general appearance and gait;
(ii) conforming to social routines and conventions;
(iii) physical appearance;
(iv) skills in presenting a favourable façade of own personality and concealing unfavourable aspects.

The following items are rated on the basis of observed behaviour:

Idiosyncratic peculiarities of gait: (Subject does ritualistic movements while walking, or swings legs in a rather peculiar way. Rate (2) when it is very noticeable and peculiar). ☐

Lack of manners: (Subject's manners are not as it would be expected from his cultural background, such as thanking, greeting, apologising, parting, etc. Rate (2) when it is very noticeable). ☐
Note: Do not include unpolished manners due to lack of social education and always take into account lack of opportunity to display manners in an interview. Rate (9) in that case.

Histrionic behaviour: (Subject talks, makes gestures in an exaggerated, dramatic, histrionic manner. Rate according to intensity and frequency). ☐

Self-neglect: (Consider subject's degree of cleanliness, state of hair, whether shaven or not, clothes, etc. Rate (1) when there is marked lack of attention to at least one of these aspects of personal appearance. Rate (2) if there is marked self-neglect in more than one aspect or if, for example, the subject smells because of self-neglect). ☐

Inappropriate dressing: (Subject is dressed up conspicuously out of fashion and not as it would normally be expected from his social background. Colours and materials do not seem to be matching altogether and the style of dressing does not fit to any kind of social subgroup (e.g. punk, rock, hippy etc.) or any fashion past or present). ☐

Irreverent behaviour: (Subject sings, makes facetious remarks or silly jokes, seems unduly familiar with the interviewer. Picks his nose or ear for long periods, etc. Rate (2) if it is present throughout the interview). ☐
Note: Write down the examples.

Embarrassing behaviour: (Due to loss of social restraints, subject exposes himself, scratches genitals, tries to make sexual suggestions and advances during the interview. Rate (1) when it occurs only on a few occasions). ☐
Note: Write down the examples.

The following items are rated to some extent as an interpretation of observed behaviour:

Bizarre appearance: (Subject wears 'secret documents', clothes or ornaments with a special significance (e.g. a hat may keep the rays off). Rate only when the odd appearance is presumed due to psychotic symptoms. Rate (2) when the whole impression is grossly odd and would be remarked upon readily). ☐

Overall impression (9 = impossible to make a rating) ☐

No disturbance: Nothing in the subject's self-presentation would leave an unfavourable impression in a normal social situation. 0
1
2
Minimum disturbance: Subject would be conspicuous and make a somewhat unfavourable impression in a normal social situation. 3
4
Maximum disturbance: Subject's self-presentation quite incompatible with a normal social situation. 5

2. Activity

2.1 Sleepiness

Consider: Abnormal drop in alertness, speed of response and initiative in the course of interview. The manifestations of sleepiness should be out of proportion to the length of the interview, or to the demands put to the patient during the examination, and should be unusual for the time of day.

The following items are rated on the basis of observed behaviour:

Drooping eyelids or head and yawning: (Rate 1) when these symptoms are intermittent and subject can control it and can stay alert. Rate (2) if the interview is frequently interrupted or cannot be carried out properly). ☐

Intermittent and/or progressive slowing down of speech and postural movements: (Subject's movements and speech gradually and/or intermittently slow down *because of sleepiness or fatiguability*). ☐

The following item is rated to some extent as an interpretation of observed behaviour:

Inability to stay mentally alert: (Subject has an intermittent and/or progressive loss of concentration, complains of tiredness, cannot pay enough attention to follow the interview *because of sleepiness or fatiguability*). ☐

Overall impression (9 = Impossible to make a rating) ☐

No disturbance: Subject normally alert throughout 0
the interview, no signs of sleepiness.
1
Minimum disturbance: Some signs of sleepiness 2
progressive or intermittent loss of concentration
during the interview, complaints of tiredness, may
look sleepy, yawns occasionally; if sufficiently 3
marked to make the continuation of the interview
difficult, rate 2 or more.
4
Maximum disturbance: Signs of extreme fatiguability
subject falls asleep; during the interview and is 5
difficult to wake.

2.2 Attention disorders

Consider: (i) Subject's ability to maintain and appropriately shift the focus of attention in relation to the topics discussed during the interview: (ii) Attention deficits may be due to failure of selective attention, or to withdrawal of attention. Failure of selective attention is shown by distractability, (i.e. turns attention to trivial noises, events outside the room, or is more pre-occupied with his physical condition or hypomanic ideas, etc). Attention withdrawal is shown by the subject being pre-occupied with internal experiences such as depression, anxiety, hallucinations or delusions.

The following two items are rated on the basis of observed behaviour:

Distractability: (Stops talking or changes subject due to distraction by trivial noises or events outside the room, or turns attention to some other topic that he is pre-occupied with). ☐

Blank spells: (Sudden stoppage or inattention while speaking for a few seconds or longer; may be due to thought blocking, hallucinations or very severe anxiety). ☐

The following two items are rated to some extent as an interpretation of observed behaviour:

Attention withdrawal as a result of lack of concentration: (Subject usually complains about having lack or loss of concentraton, asks for questions to be repeated, although he is generally willing to turn his attention to the topic discussed, but is not *able* to do so, usually due to anxiety or depression). ☐

Attention withdrawal due to behaviour resulting from hallucinations: (i.e. lips move soundlessly, looks around, giggles, etc). ☐
Note: Include also reasonable presumptions that the interferring behaviour is caused by hallucinations.

Overall impression (9 = impossible to make a rating) ☐

No disturbance: Subject completely in touch with the 0
interviewer throughout the interview.
1
Minimum disturbance: Some effort is necessary to 2
attract or maintain the subject's attention to the topics
of the interview, but no major difficulty.
3
Maximum disturbance: Interview grossly affected or 4
almost impossible because subject's attention is
severely disturbed. Subject is almost completely 'out
of touch' and inaccessible. 5

2.3 Psychic tempo

2.3a *Decreased*

Consider: Reduction of rate, speed and extent of voluntary movements: delays in responding to questions or initiating tasks or movements requested of patients; your overall impression of the speed of mental processes of the patient.

The following items are rated on the basis of observed behaviour:

Slowness of limbs and body: (Delay in performing movements sits abnormally still, walks abnormally slow. Do not rate 2, unless there is an almost total absence of movements throughout the interview). ☐
Note: Do not rate stillness here unless it accompanies psychic slowness.

Slow speech: (Long pauses before answering, long pauses between words. 1 = fewer than 10 pauses in all, 2 = long pauses throughout the interview). ☐
Note: Only long pauses are rated here; drawling and slow articulation are rated in section 4.2.

The following item is rated to some extent as an interpretation of observed behaviour: (The individual components of this item are observation, but the rating itself represents the observer's conclusion that the overall syndrome is best called stupor).

Stupor: (Total or near total lack of voluntary movement and/or muteness, but with evidence of relative preservation of conscious awareness). ☐

Overall impression (9 = impossible to make a rating) ☐

No disturbance: Subject's movements are not different 0
from an average healthy person's movements in
similar conditions. 1
Minimum disturbance: Retardation of either body
movements or speech, *or* some retardation in all these 2
respects.
3
Maximum disturbance: Subject extremely slow in
every respect, to the extent of stupor; has to be led 4
to the interview room; may answer some questions
after long delays and repeated prompting.
5

2.3b Increased

Consider: Increase in rate, speed and extent of voluntary movements and speech.

The following items are rated on the basis of observed behaviour:

Increased speed of movements of limbs and body: (Subject performs movements rapidly, changes body position frequently, walks or paces abnormally quickly). ☐
Note: Items like restlessness, pacing and frequent unnecessary movements which are not in themselves carried out at an increased tempo, are not rated here.

Pressure of speech: (More copious and rapid speech than normal, unnecessary words are added frequently. Rate (2) when the whole interview is markedly characterised in this way). ☐
Note: This item is only concerned with the speed of the speech rather than the speed of ideas (rate Flight of ideas in Section 4.2.c).

Overall impression (9 = impossible to make a rating) ☐

0
No disturbance: Subject's movements are not different from an average healthy person's movements in similar conditions. 1
2
Minimum disturbance: Increased body movements or speech, but not in an extreme level. 3
4
Maximum disturbance: Subject moves or talks extremely fast. 5

2.4 Initiative

2.4a Abnormal lack of initiative

Consider: The lack of manifestations independent of unprompted acting and self-determination during the interview, including expression of personal opinion, situation — relevant acts (e.g. closing the door, lifting an object from the floor) asking questions of the interviewer, asking for permission to smoke, wondering about the purpose of interview or about things in the interview room etc.
Note: It is likely that in an interview, the subject may not have the opportunity to manifest the whole potential of initiative he has. So a rating of (9) may be quite common. Some subjects can lose initiative because of their neurotic symptoms and pre-occupation with their problems, while some others lose theirs with psychotic symptoms and the denial of any problems. Both these types of loss of initiative are included here.

The following items are rated on the basis of observed behaviour:

Lack of expression of personal opinion: (Regardless whether the opinions appear to be reasonable or agreeable to the interviewer or not, they should be considered as opinions. Rate subject's inability to express his opinions about the situation, the interview, room, etc). ☐

Tendency to agree passively or avoid the interviewer's questions without regard to their content: (Subject says 'yes', 'I suppose so', 'don't know', 'not sure' etc. repeatedly to such an extent or in such a way that the interviewer concludes that they are not giving specific replies to each question). ☐

Abnormal lack of spontaneous complaints or criticisms: (Rate subject's inability to make criticisms or complaints about the general immediate environment e.g. the interviewer, interview, lights, room treatment etc). ☐

Absence of situation-relevant acts: (Subject is not able to manifest initiative even when there are appropriate occasions as mentioned above). ☐
Note: Take account of greetings and partings with interviewer outside the immediate interview situation. This item records simply the presence or absence of these acts, not the skill or completeness with which they are carried out; these qualities are rated under Section 1, 'self-presentation'. If no such occasion is present, rate 9.

Overall impression (9 = impossible to make a rating) ☐

0
No disturbance: subject shows as much initiative as it would be culturally normal in an interview. 1
2
Minimum disturbance: manifestations of initiative do not occur although there were appropriate occasions. 3
4
Maximum disturbance: total lack of initiative, passive compliance. 5

2.4b Abnormal excess of initiative

Consider: Manifestations of initiative are excessive and noticeable, subject's behaviour is inappropriate and disrupts interview, moves round to check things in the room or changes the places of them, brings out his personal opinions about the interview, interviewer, treatment quite often, makes lists of demands etc.

Items in this section are rated on the basis of observed behaviour:

Excessive expression of personal opinion: (Subject manifests his own opinions more than it is appropriate during an interview (rate = 1), or excessive enough to seriously disrupt the interview (rate = 2)). ☐

Excessive disagreement with the interviewer: (Rate when subject persistently and disruptively disagrees with the interviewer). ☐
Note: Dot not include appropriate negative replies to the interview questions.

Making too many requests or demands: (Subject gives lists of requests and demands more than it is appropriate (rate = 1), or excessive enough to seriously disrupt the interview (rate = 2)). ☐

Presence of too many complaints or criticisms: (Rate when subject complains about being interviewed, is *persistently* critical of individual questions, complains about the interviewer, room, lights, etc). ☐

Lack of proper concern with the interview and the interviewer: (Subject moves around to change the places of things, seems unexpectedly relaxed, or if he is being interviewed at home, continues to do his work or watches TV etc. *and* does not pay enough attention to the questions). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject shows as much initiative as it would be culturally normal in an interview. 0
1

Minimum disturbance: Subject manifests over-initiative but interview can proceed with some effort. 2
3

4
Maximum disturbance: Subject's behaviour is definitely inappropriate and disrupts the interview. 5

3 Display of affect

3.1 Display of quantity of affect

Consider: This section is involved with the ratings of quantity of emotions and rate of changes, irrespective of the individual emotion shown which will be dealt with in the following Section (3.2).

The following items are rated on the basis of observed behaviour:

Reduced quantity and/or range of expressive facial and bodily movements: (Consider the total number of instances of expressive movements, irrespective of the type of emotion displayed). ☐

Increased quantity and/or range of expressive facial and bodily movements: (Subject shows an unusual amount or wide range of expressive movements, but not necessarily the rapid change specified in the item below). ☐

Lability of mood: (Consider the rapidity and frequency of changes of mood). ☐

Gross excitement: (Throws things, runs, jumps around, waves arms wildly, shouts, screams. Rate (1) if only one brief episode after which subject calms down and interview can proceed. Rate (2) if more than one episode or if more continuous). ☐

Blunted affect: (Expressionless face and voice, lack of responding emotionally to distressing topics. If severe and fairly uniform throughout the interview rate (2). Rate (1) if severe but less uniform). ☐

Note: Subjects with blunted affect may still show emotions in a few instances during the interview.

Overall impression (9 = impossible to make a rating) ☐

No disturbance: Subject's affective display is not different from an average healthy person's display of affect in similar circumstances. 0
1

Minimum disturbance: Face tends to be either less expressive or to show occasionally rather unusual changes. This would be regarded as unusual in subject's normal social setting, but not particularly disruptive or distressing to others. 2
3

Maximum disturbance: Gross abnormalities about the quantity of emotions and rate of changes. Would make very unpleasant and disturbing impression on others and could be socially disruptive or unacceptable. 4
5

3.2 Display of quality of affect

Consider: This section is involved with the nature and quality of emotions. Rate the observed manifestations of affect and mood.

Note: Positive ratings of observed anxiety and/or depression should not be made if blunted affect (Section 3.1) is rated as present to a marked degree, but they are regarded as compatible with ratings of blunted affect of mild or moderate degree; this combination implies variability in affect shown during the interview.

The following items are rated on the basis of observed behaviour:

Observed anxiety: (Tense, worried look or po posture, fearful apprehensive look, blushing, tremor, frightened tone of voice. Rate (2) when subject shows anxiety more or less throughout the interview). ☐

Note: Examinations itself may provoke anxiety, do not rate as present, if in doubt.

Observed depression: (Sad, mournful look, tears, gloomy tone of voice, deep sighing voice chokes on depressing topics or apparently 'frozen misery'. Rate (2), when he cries openly or demonstrates depressive signs frequently throughout the interview). ☐

Hypomanic affect: (Unduly smiling and cheerfully euphoric, elated. Rate (2), when the subject is highly elated or exalted). ☐

Hostile irritability: (Un-cooperative, irritable, angry, overtly hostile, discontented, naughty, antagonistic. Rate (2), when the interview has to be discontinued because of irritability). ☐

The following item is rated to some extent as an interpretation of observed behaviour:

Perplexity: (Looks puzzled, cannot explain or understand his experiences). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject's affective display is not different from an average healthy person's display of affect in similar circumstances. 0 1

Minimum disturbance: An abnormality in any one of the areas described above is present in a moderate form. 2 3

Maximum disturbance: The interview is disrupted by severe degrees of disturbance of one or more of the affects above. 4 5

3.3 Other disturbances of facial expression

Consider: This section is involved with some other characteristics of facial expression which are not a matter of quantity alone and more complicated in nature.

The following items are rated on the basis of observed behaviour:

Gaze avoidance: (Rate subject's avoidance of mutual glance, i.e. eye contact with interviewer or avoidance of looking at interviewer while listening or talking). ☐

Abnormal staring: (Prolonged periods of eye fixation at interviewer, culturally inappropriate. Rate (2) if it would leave a grossly unfavourable impression.) ☐

Facial mannerisms or stereotypies: (Distinct idiosyncratic or repetitive movements of unclear meaning, grimacing, etc., not classifiable as tics or automations). ☐

Involuntary facial movements: (e.g. facial tics, masticatory movements, etc). ☐

The following items are rated to some extent as an interpretation of observed behavour:

Inappropriateness: (Non-correspondence between facial expression and reported or inferred inner experience). ☐
Note: Bear in mind that a person does not necessarily have to look sad or unhappy all the time when talking about unpleasant topics, particularly if they recur several times in the interview.

Incomprehensibility: (Occurrence of facial expressions which the interviewer cannot 'read' or recognise as indicating the presence of a particular emotion). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject's affective display is not different from an average healthy person's display of affect in similar circumstances. 0 1

Minimum disturbance: Face tends to show rather unusual expressions in a mild or moderate form, but this would not be regarded as distressing or disruptive to others. 2 3

Maximum disturbance: Unusual expressions are continuous and present in a markedly obvious form and would leave an unpleasant and disruptive impression on others. 4 5

4 Communication skills

4.1 Communication by 'body language'

Consider: (i) The posture and gestures of subject during interview (e.g. indicating openness for communication or distance and 'turning away' from interviewer, etc); (ii) amout and range of expressive gestures; (iii) presence/absence of idiosyncratic or symptomatic patterns of body movements).
Note: Slowness of limbs and body should not be rated here (see Section 2.3.a)

The following items are rated on the basis of observed behaviour:

Stillness in body positions: (Subject sits in one position for long periods of time in a somewhat abnormal way, *without* either being necessarily slow in psychic tempo, *or without* suggesting an uncommunicative or hostile attitude to interviewer). ☐

Abnormally limited use of gestures in frequency and range: (Subject does not use gestures as it would normally be expected from his particular cultural background). ☐

Abnormally relaxed posture forms: (Predominates during the interview, subject sits or lays down too relaxed in a rather culturally inappropriate way). ☐

Restlessness: (Subject is fidgety, restless, paces up and down, does frequent unnecessary movements, but does not perform any repetative movements). ☐
Note: On some occasions, actions like folding arms or holding legs together, etc, can be the signs of control over restlessness. Rate (1) when there is controlled restlessness.

Movement due to obsessional urges: (An irresistible urge to perform an apparently unreasonable act repetitiously. Subject may have compulsive rituals such as touching or counting things, or may stay with his arms folded in order to avoid germs, dirt, etc.). ☐

Involuntary body movements: (e.g. tics, tremors, dyskinesias, dystonias, chreoathetosis). ☐

Mannerism and posturing: (Odd, stylised movements or acts, usually idiosyncratic to the subject, sometimes suggestive of special meaning or purpose; uncomfortable or inappropriate postures, e.g. subject salutes various times or makes complex gestures with his hands, etc.) ☐

Stereotypies: (Persistent and constant repetition of movements or postures such as rocking to and fro on a chair, rubbing head round and round with the hand, nodding head, etc. But these movements do not seem to have special significance for the subject). ☐

Catatonic movements: (Subject demonstrates one or more of these: Negativism (doing the opposite of what is asked), ambitendence (fluctuation between two alternatives), echopraxia (imitation of body movements), echolalia (imitation of words or phrases), flexibilitas cerea, mitgehen (excessive co-operation in passive movement). If organic cause suspected, rate (9). ☐

The following items are rated to some extent as an interpretaton of observed behaviour:

Predominance of abnormally reclined or closed posture: (Suggesting an incommunicative or hostile attitude, e.g. subject turns away at 90° angle to interviewer). ☐

Rigidness in posture: (Rate when subject manifests a rather rigid looking posture predominantly). ☐

Withdrawn posture: (Subject's body posture is again reclined and closed, but the reason for this is to be withdrawn rather than hostile). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Body movements are expressive 0
within the range of what is culturally expected and
acceptable.
Minimum disturbance: Some abnormality in either 1
posture, body orientation forms, or use of gestures,
as well as some voluntary movements may be present;
but no gross overall disturbance and no catatonic 2
phenomena, stereotypies, mannerisms or posturing.
If several of the areas listed above indicate a
disturbance, rate 2 or more. 3

Maximum disturbance: Grossly reduced or absent or 4
bizarre use of gestures; constant or severe catatonic
signs, stereotypies; or constant and severe involuntary
movements. 5

4.2 Verbal communication-conversation

4.2.a *Decreased elements of conversation*

Consider: (i) The reduced elements in the quality of voice and delivery, (ii) amount and flow of speech, (iii) lack of contained information, (iv) lack of humour and interaction with the interviewer in conversation. Note: If muteness is rated as present, rate only item (listener's feed-back) in this section, fill in 9s in the remaining boxes.

All the items in this section are rated on the basis of observed behaviour:

Muteness: (Rate (1) when subject says no more than twenty words in all, rate (2) when totally mute and inaccessible). ☐

Restricted quantity of speech: (Subject frequently fails to answer and does not use extra sentences or unprompted additional comments. Rate (1), when it is difficult to keep conversation going. Rate (2) when the answers are restricted to the minimum, e.g. often one word or telegrammatic style). ☐

Abnormally quiet voice: (Subject talks so quietly that it is very difficult to hear. Rate (2) if this would make a very disturbed effect on others). ☐

Abnormally flat tone of voice: (Subject talks with a very monotonous tone of voice, almost no expression of emotion or modulation is seized. Rate (2) when it is very noticeable and disturbing). ☐

Drawling and slow articulation: (Subject pronounces words slowly and sound of vowels are longer than usual, but it is not necessarily difficult to understand. Rate (2) when it would make a very disturbed effect on others). ☐

Poverty of content of speech: (Subject talks freely, but no information is given in spite of the number of words used, and is not able to recapture the topic he talks about. Rate (2) when it is very difficult to get any useful information through the interview). ☐
Note: Make due allowance for poor education or intelligence, or use of language.

Lack of humour: (Subject does not show any humour although conversation offers appropriate occasions. Rate (2) when he gets openly angry over jokes or humorous situations). ☐
Note: Ratings of 9 can be expected quite often as the occasions to show humour are most unlikely to happen in an interview situation.

Disturbance of listener's feedback: (Subject shows lack of signals listeners normally omit, like looking up, affirmative nodding, phrases like 'I see' . . . 'Is that so?' etc. Rate (2) when showing no signs of listening would make a very disturbed effect on others. ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject's conversational skills 0
unimpaired.
1
Minimum disturbance: Conversation with subject is
somewhat difficult but can proceed if interviewer 2
makes some effort.
3

Maximum disturbance: Subject is practically unable 4
to engage in a conversation, (but is not mute; rate 9, if
subject does not talk at all). 5

4.2.b *Increased elements of conversation*

Consider: (i) The increased elements in the quality of voice, (ii) the length and the amount of speech.

All the items in this section are rated on the basis of observed behaviour:

Abnormally loud voice: (Subject talks very loudly as though others are not able to hear. Rate (2) if this would make a markedly disturbed effect on others). ☐

Abnormally lengthy and circumstantial speech: (Subject talks in too much detail and is difficult to interrupt. Rate (1) when it happens in more than a few occasions. Rate (2) when the interview cannot proceed properly). ☐

Silly jocularity: (Subject makes jokes and laughs even at inappropriate occasions. Rate (2) when the whole conversation is interlarded with jokes which unable the interview to proceed properly). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject's conversational skills are unimpaired. 0
1
2
Minimum disturbance: Conversation with subject is somewhat difficult but can proceed with some effort. 3
4
Maximum disturbance: Subject's conversation would make a very disturbed effect on others in a normal social situation. 5

4.2.c *Other elements of conversation*

Consider: (i) The quality and the flow of speech (ii) appropriateness of the interaction with interviewer in conversation.

All the items in this section are rated on the basis of observed behaviour:

Stuttering or stammering: (Rate (1) when subject stutters occasionally or only does so on particular topics. Rate (2) when he stutters or stammers during the whole interview). ☐

Slurred and sloppy speech: (Subject pronounces words in a slurred and sloppy way but this may not be necessarily difficult to understand. Rate (2) when it is to a marked degree and takes extra effort to be understood properly). ☐

Disturbance of articulation: (Subject shows any form of dysarthria, i.e. articulation is jerky, hesitant or slurred). ☐

Mumbling: (Subject's speech is low-pitched and partly indistinct. Rate (2) if mumbling is persistent and not clearly connected with replies to the questions that have just been asked). ☐

Non-social speech: (Subject mutters or whispers to self spontaneously, moves lips soundlessly or shouts 'to voices', etc., and the context of the speech does not fit within the social context of the interview and is *not* addressed to the examiner. Rate (2) when the interview cannot proceed). ☐

Simultaneous talking or talking out of turn: (Subject talks simultaneously, or interupts the interviewer. Rate (1) when there are more than a few occasions. Rate (2) if the interview cannot proceed properly). ☐

Pre-occupation with symptoms or other certain topics: (Subject is not able to attend a variety of topics of conversation and tends to return repeatedly to his own topic. Rate (2) when it is very difficult to proceed the interview). ☐

Perseveration: (Subject gets stuck by repeating phrases or individual words. Rate (2) when it is extremely difficult to proceed the interview). ☐

Incoherence: (Subject has distorted grammar, answering beside the point, lack of logical connexion, sudden irrelevances. Rate (1) when there is a lesser degree of incoherence so that some of the subject's meaning does get through). ☐
Note: Write down the examples.

Flight of ideas: (Subject's ideas move from one theme to another and can be fairly easy to follow. There may also be Clang associations which are associations of words by sound or rhyme. Rate (1) if it is marked but is still possible to grasp some of the subject's meaning and to proceed the examination. Rate (2) when it is difficult to conduct a useful interview at all). ☐
Note: Write down the examples.

Neologisms and idiosyncratic use of words or phrases: (Subject makes up words which have no generally accepted meaning or uses ordinary words or phrases in an unusual way. Rate (1) if only a few examples. Rate (2) if whole conversation is interlarded with them). ☐
Note: Write down the examples.
Overall impression: (9 = impossible to make a rating) ☐

No disturbance: Subject's conversational skills are unimpaired. 0
Minimum disturbance: Conversation with subject is somewhat difficult but can proceed with some effort. 1
There are articulation problems to a lesser degree. 2
Maximum disturbance: Subject is practically unable to engage in a conversation, either has very severe degrees of articulation problems or very marked perseveration or flight of ideas of neologisms. 3
4
5

5 Co-operation

Consider: The mutual relations of the subject with the interviewer (and presumably with the other people), and the degree of co-operation during the course of the interview.

The following two items are rated on the basis of observed behaviour:

Suspiciousness: (Subject feels that everything is not as it should be and thinks that there may be a deliberate attempt to harm or annoy. Looks around, checks things, asks questions etc. Rate (1) if the subject shows suspicion but is not openly suspicious of the interview procedure. Rate (2) when the subject is also suspicious of the interviewer and the interview). ☐

Hostility: (Subject uses different ways of showing hostility. He can be overtly angry and hostile or may use subtle ways such as cutting off the interviewer by saying 'no' before the question is finished. Rate (2) when he is openly angry and/or the interview cannot be conducted because of hostility). ☐

The following two items are rated to some extent as an interpretation of observed behaviour:

Misleading answers: (Subject answers 'yes' or 'no' to questions, or frequently contradicts the self, and appears to be deliberately misleading. Rate (1) when only some of the replies seem to be misleading. Rate (2) if marked so that it is difficult to trust any of the ratings). ☐

Verbal over-compliance: (Subject says 'yes' or 'no' repeatedly without being deliberately misleading. He is passively submissive or replies in such a way that it is clear that he is mainly trying to please the interviewer or to avoid giving detailed and specific replies to the questions). ☐

Manifest resentment of the interview: (Subject seems unwilling to co-operate, talks very reluctantly, seems apathetic or listless without being hostile to interviewer. Rate (2) if marked throughout the interview). ☐

Overall impression: (9 = impossible to make a rating) ☐

No disturbance: (Subject co-operates adequately). 0

Minimum distirbance: Subject shows some resistance 1
and unwillingness to co-operate with interviewer but
interview can proceed with some effort. If marked 2
suspiciousness and hostility, or misleading answers
Rate (2) or more. 3

Maximum disturbance: Interview practically 4
impossible due to subject's refusal to co-operate
and hostility. 5

If this person has any impairment in this schedule, specify the predominant cause or causes from the following list, according to your clinical impression:

(tick)

Due to physical illness (specify) .... ☐
Specify code number of items affected ....

Due to drug effect (specify) .... ☐
Specify code number of items affected ....

Due to personality trait (specify) .... ☐
Specify code number of items affected ....

Due to neurosis (specify) .... ☐
Specify code number of items affected ....

Due to functional psychosis (specify) .... ☐
Specify code number of items affected ....

Due to organic psychiatric condition (specify) .... ☐
Specify code number of items affected ....

None (person may not have any morbid condition but still may be rated positively on some of the items in this schedule; please comment and specify items rated). ☐
Specify code number of items affected ....

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Rating of Negative Symptoms Using the High Royds Evaluation of Negativity (HEN) Scale

A.M. MORTIMER, P.J. McKENNA, C.E. LUND and S. MANNUZZA

The concept of deterioration has always been central to schizophrenia, and forms a cornerstone of current diagnostic and conceptual thinking (e.g. DSM–III; Crow, 1985; Weinberger, 1987). Recently, there has been a renewal of interest in the deficits of schizophrenia, with attempts to identify, classify, and measure the relevant abnormalities. According to current thinking (Crow 1985; Wing, this volume) negative symptoms i.e. deficits in emotion, volition and social interaction, represent a distinctive cluster of impairments with aetiological, prognostic and therapeutic significance. Verification of this view of course requires reliable and valid measures of negative symptoms.

Several scales have become available for the study of negative symptoms (Abrams & Taylor 1978; Andreasen 1982; Iager *et al*, 1985). It was, however, felt that each had certain disadvantages, and an attempt could be made to combine the best points of each. For instance the Scale for the Assessment of Negative Symptoms (SANS) of Andreasen (1982) has been validated by extensive research use but is rather long (42 items) and requires accessory information from an informant. Some items require self-rating of negative symptoms which schizophrenic patients may find difficult and which is of questionable usefulness.

The High Royds Evaluation of Negativity (HEN)

The new scale aimed to be detailed but quick and easy to use, without needing an informant, and as objective as possible. To generate items the classical and contemporary literature was searched for descriptions of deficit symptoms. A particular emphasis of the study was the detailed evaluation of abnormal affectivity as judged directly. Groups of psychiatrists were then asked to rate patients live or on video, and it quickly became apparent which ratings were practicable.

Initially 32 items were derived and divided into six straightforward categories: appearance, behaviour, speech, thought, affect, and functioning. Each item was rated on a 5-point scale from 0 (normal) to 4 (severe). Guidelines and anchor points were devised where possible. Each category contained a 'global' item rated impressionistically according to the scores on the preceding items. This was found to increase reliability. A summary score consisting of the sum of the six 'globals' provided an overall measure of the severity of negative symptoms.

Like most procedures the administration of the scale became easier with a little practice. Eventually 5–10 minutes with the patient sufficed; the scale was particularly suitable for administration immediately following other ratings (e.g. of positive symptoms). This preliminary scale was refined using a combination of reliability and validity studies.

Reliability

Preliminary scale

Fifty patients with a clinical diagnosis of schizophrenia were rated independently by three interviewers. Patients were drawn from a range of settings including acute, rehabilitation and 'back' wards. Kendall's tau measure of inter-rater reliability was used initially; most items showed fair to good reliability with tau = 0.69–0.73. Three of the four original aspects of affect could be reliably distinguished, although the item Shallow/coarsened affect was initially liable to be confused with Inappropriate affect.

Some items with poor reliability (e.g. Sits unnaturally still) were dispensed with; others were provisionally retained but separated for special study (notably Poverty of content of speech and Inappropriate affect).

Revised scale

Thirty patients with a DSM–III/RDC diagnosis of schizophrenia from out-patient and in-patient settings were then rated independently by three raters working in pairs. Kendall's W concordance measure was used to reassess inter-rater reliability; all items showed good/excellent reliability, W = 0.72–0.99. Global items were as expected more reliable than individual items (see Table I). The separately rated items Inappropriate affect and Poverty of content of speech continued to show poor reliability, and the former emerged as being of dubious validity; both these items were therefore deleted from the final version of the scale.

TABLE 1

Kendall's coefficient of concordance W for inter-rater reliability

Appearance		
face/hair	$W = 0.92$	$P = 0.01$
body	$W = 0.93$	$P = 0.01$
clothes	$W = 0.94$	$P = 0.01$
global appearance	$W = 0.01$	$P = 0.01$
Behaviour		
reduced facial expression	$W = 0.80$	$P = 0.05$
reduced gestures	$W = 0.90$	$P = 0.01$
slow/clumsy	$W = 0.77$	$P = 0.06$
global behaviour	$W = 0.88$	$P = 0.02$
Speech		
reduced speech	$W = 0.88$	$P = 0.22$
lacks inflection	$W = 0.87$	$P = 0.02$
slow rate	$W = 0.75$	$P = 0.07$
global speech	$W = 0.95$	$P = 0.01$
Thought		
poverty of thought	$W = 0.80$	$P = 0.05$
attention impaired	$W = 0.91$	$P = 0.02$
global thought	$W = 0.77$	$P = 0.06$
Affect		
constricted affect	$W = 0.86$	$P = 0.03$
withdrawn	$W = 0.72$	$P = 0.09$
facile affect	$W = 0.72$	$P = 0.09$
global affect	$W = 0.77$	$P = 0.04$
Functioning		
reduced interests	$W = 0.93$	$P = 0.01$
social withdrawal	$W = 0.91$	$P = 0.02$
sexual interest	$W = 0.90$	$P = 0.02$
work impairment	$W = 0.94$	$P = 0.01$
global function	$W = 0.92$	$P = 0.01$

Validity

Face validity

Forty-nine in-patients with a clinical diagnosis of schizophrenia were rated on the HEN and independently rated by nurses on the Social Behaviour Scale (SBS) of Wykes & Sturt (1986). This well validated scale contains items which describe negative symptoms e.g. Inability to start a conversation, items which describe positive symptoms e.g. Responding to hallucinations, and others which describe non-specific or unclassifiable symptoms. The nurse raters had known the patients for months if not years and were thus able to provide 'longitudinal' as opposed to 'cross-sectional' judgements.

Face validity of the HEN should be demonstrable by a correlation with SBS negative symptom scores but not with SBS positive scores (in each case the scores represented the sum of scores of individual items). A highly significant positive correlation between HEN summary score and SBS negative ($r = 0.66$; $P = < 0.001$) was found but there was no correlation ($r = 0.05$; NS) with SBS positive score.

Criterion validity

Individual HEN item scores were correlated with the HEN summary scores (sum of 'globals') in 64 schizophrenic patients from both wards and out-patient clinics. All main scale items were highly significantly correlated with the summary score with $P = < 0.001$ for every item. Some of the items rated separately correlated less well with the summary score but still with significance; in particular Poverty of content of speech showed a correlation of 0.43 ($P = 0.01$). Inappropriate affect, on the other hand, showed no significant correlation with the summary score, ($r = -0.11$) as found previously (Andreasen & Olsen, 1982).

Further tests of validity

The 'global' scores of the six categories of the scale were significantly intercorrelated. The highest correlations were between Global thought with both Global behaviour and Global speech ($r = 0.72$, $P = < 0.001$); the lowest was between Global appearance and Global speech ($r = 0.23$, $P = 0.04$).

The validity of the groupings of items in each category was tested using a cluster analysis from the SPSS-X package. At the two cluster solution Inappropriate affect Shallow coarsened affect, and Poverty of content of speech split off from the rest of the items. At the three cluster solution the remaining items split into a speech, affect, and behaviour cluster versus an appearance, function, and thought cluster. Subsequent splits showed a strong tendency to divide the items categorywise.

In conclusion the HEN emerges as a reliable, valid and detailed measure of negative symptoms, which had the added advantages of being fast and easy to use. This study also documents the syndromal status of negative symptoms, that is their pronounced tendency to occur in association with each other (see also Andreasen, this volume). As found previously, the symptom of inappropriate affect did not seem to represent a negative symptom (Andreasen, 1982). Poverty of content of speech emerged as difficult to rate reliably and its validity as a negative symptom appeared suspect; further work is needed to establish its status.

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High Royds Evaluation of Negativity (HEN III)*

?. not assessed
0. Absent
1. Questionable
2. Mild
3. Moderate
4. Severe (in general, reserved for chronically hospitalised patients)

1. Appearance

1. Face and hair (unwashed, unshaven), hair unkempt, poor dental state. (Not wearing dentures = at least 2)
   ? 0 1 2 3 4
2. Body (dirty nails, nicotine stained fingers, body odour)
   ? 0 1 2 3 4
3. Clothes (soiled, torn, missing buttons, holes in shoes, broken/untied shoelaces. Hospital charity shop clothes) = 3 or 4
   ? 0 1 2 3 4
4. *Global rating of appearance*
   ? 0 1 2 3 4

2. Behaviour

5. Reduced facial expression (rate normal animation only; disregard grimacing, dyskinesia)
   ? 0 1 2 3 4
6. Reduced expressive gestures (rate normal gestures only; disregard stereotypies, mannerisms, dystinesia)
   ? 0 1 2 3 4
7. Slowness/clumsiness of movement (lack of normal ease, naturalness of movement, sits abnormally still)
   ? 0 1 2 3 4
8. *Global rating of behaviour*
   ? 0 1 2 3 4

3. Speech

9. Reduced in quantity (poverty of speech; *distinguish from item 13*)
   ? 0 1 2 3 4
10. Lacks inflection (lacks normal modulation; monotonous; include harsh or stereotyped inflection)
   ? 0 1 2 3 4
11. Slowness/latency of speech (measured, ponderous, laboured speech; *include latency of responding*)
   ? 0 1 2 3 4
12. *Global rating of speech*
   ? 0 1 2 3 4

4. Thought (Do not rate unless speech output adequate)

13. Impoverishment of thought (ideas conveyed in a repetitive, stereotyped way; keeps returning to same themes; poverty of ideation)
   ? 0 1 2 3 4
14. Poor performance of tests of attention/concentration (e.g. months backward; serial sevens; take educational background into account)
   ? 0 1 2 3 4
15. *Global rating of thought*
   ? 0 1 2 3 4

5. Affect

16. Constricted affect (reduced range of emotional expression; lack of responsiveness to social cues; indifference to emotive e.g. delusional topics)
   ? 0 1 2 3 4
17. Emotional withdrawnness (cold, aloof, vacant, lack of rapport)
   ? 0 1 2 3 4
18. Shallow/coarsened affect (emotions lack subtlety, depth or conviction; 'superficial', 'facile'; *do not rate inappropriate affect, causeless laughter etc*)
   ? 0 1 2 3 4
19. *Global rating of affect*
   ? 0 1 2 3 4

6. Functioning (Past month or immediately prior to most recent admission, if acute)

20. Reduced interests (0/1 = some active interests, goes out, or keeps occupied; 2 = more passive interests, like reading, music; 3 = passive TV watching only; 4 = no interests, does not take in TV, if watched)
   ? 0 1 2 3 4
21. Social withdrawal (0/1 = actively seeks company; 2 = social life limited, e.g. to family; 3 = passive socialisation, e.g. visits from relatives; 4 = no interest in socialisation or relatives visits)
   ? 0 1 2 3 4
22. Reduced sexual interest (0/1 = within normal limits for age, sex, circumstances; 2 = disproportionately diminished; 3 = minimal; 4 = total absence of interest or activity. *Use judgement and make allowances*)
   ? 0 1 2 3 4
23. Work impairment (0/1 = working regularly/part-time; 2 = working irregularly; 3 = unemployed or in hospital rehab. scheme; 4 = incapable of work, though may attend OT. If housewife, rate 0–3 on ability to perform house duties)
   ? 0 1 2 3 4
24. *Global rating of functioning*
   ? 0 1 2 3 4
25. *Summary score* (sum of global ratings)
   0–24

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Neural Mechanisms of Negative Symptoms

NANCY C. ANDREASEN

When Kraepelin originally defined and described dementia praecox, he assumed that it was due to some type of neural mechanism. He hypothesised that abnormalities could occur in a variety of brain regions, including the prefrontal, auditory, and language regions of the cortex. Many members of his department, including Alzheimer and Nissl, were actively involved in the search for the neuropathological lesions that would characterise schizophrenia. Although Kraepelin did not use the term 'negative symptoms', he describes them comprehensively and states explicitly that he believes the symptoms of schizophrenia can be explained in terms of brain dysfunction:

> "If it should be confirmed that the disease attacks by preference the frontal areas of the brain, the central convolutions and central lobes, this distribution would in a certain measure agree with our present views about the site of the psychic mechanisms which are principally injured by the disease. On various grounds, it is easy to believe that the frontal cortex, which is specially well developed in man, stands in closer relation to his higher intellectual abilities, and these are the faculties which in our patients invariably suffer profound loss in contrast to memory and acquired ability." Kraepelin (1919, p. 219)

In spite of Berrios' attribution of the concept of negative symptoms to Reynolds, Hughlings-Jackson was the earliest to use the term in more or less its current meaning. (Berrios, 1985; Hughlings-Jackson, 1931). Jackson definitely suggested that negative symptoms represent a loss of function ('negative mental symptoms answer . . . to the dissolution') while positive symptoms are release phenomena that represent the exaggeration of normal functions ('the outcome of activity of nervous elements untouched by any pathological process . . . that . . . arise during activity on the lower level of evolution remaining').

While many other British and American investigators have used the terms 'negative' and 'positive', Crow (1980) was the first to articulate a comprehensive hypothesis concerning the relationship between positive and negative symptoms and other major phenomenological correlates such as premorbid functioning, response to treatment and underlying neural mechanisms. Crow's original hypothesis is similar to Jackson's, although considerably more comprehensive. Crow suggested that positive symptoms are associated with good premorbid functioning, acute onset, normal cognition and good response to treatment, a pattern of symptoms that reflected hyperdopaminergic activity in a structurally normal brain. Negative symptoms, on the other hand, were associated with poor premorbid functioning suggesting a pathological process beginning early in life, impaired cognition, and poor response to treatment, and they represented a more irreversible and ultimately structural brain abnormality produced through neuronal loss.

These early hypotheses are continuing to be tested, and therefore are continuing to evolve. They have suggested a number of important ideas that have been useful in guiding directions in the search for neural mechanisms of schizophrenia. They raise such questions as: Do negative symptoms reflect actual loss of nerve cells? If the pathological process begins early in life, could it be due instead to neuronal dysgenesis? Is the atrophy (or dysgenesis) diffuse, or does it selectively affect particular brain regions?

The search for the relationship between negative symptoms and their underlying neural mechanisms is confounded by a number of problems. Any comprehensive theory concerning the mechanisms producing negative symptoms must take a number of factors into account. First, the cross-sectional mixture of positive and negative symptoms in many patients must be explained. A simple model of neuronal loss v. hyperdopaminergic transmission cannot explain this mixture easily. Further, the model must take into account the fact that the symptoms of schizophrenia change in any given patient over time. Some patients present initially with negative symptoms, and later develop positive symptoms, while the reverse pattern occurs in others. The problem is further complicated by the confounding effects of secondary negative symptoms; that is, some patients appear to have negative symptoms as a consequence of a core neural deficit, while in others the negative symptoms are a consequence of positive symptoms: patients may withdraw socially, exhibit impoverished speech, and become affectively blunted as a consequence of hearing threatening voices or experiencing terrifying delusions. In these cases, core negative symptoms and secondary negative symptoms cannot be distinguished cross-sectionally; they can only be identified if the positive symptoms remit and the negative symptoms remain. A final difficulty is the structural and neurochemical complexity of the central nervous system. Different specific brain regions are functionally specialised, and their activity is mediated by a variety of neurotransmitter systems that have complex reciprocal interconnections. These have not as yet been fully mapped in the human brain.

Positive and negative symptoms: mechanisms and models

One reasonable working model is that originally suggested through the work of Jackson and implied in the speculations of Kraepelin. This model postulates that negative symptoms represent a loss of or decrease in normal functions, while positive symptoms represent a distortion or excess of normal functions. These abnormalities are not diffuse throughout the brain, but instead represent abberations in neural mechanisms in specific brain regions.

The negative symptoms of schizophrenia may represent a loss of functions that are generally thought to reside in the frontal lobes. Alogia is a loss of fluency of thought and speech, affective blunting a loss of the fluency of emotional expression, avolition a loss of volition and drive, anhedonia-asociality a loss of hedonic capacity, and attentional impairment a loss of the capacity to focus and sustain attention. All of these functions are normally mediated through the prefrontal cortex (Nauta, 1971; Fuster, 1980; Goldman-Rakic, 1984; Stuss and Benson, 1986). Therefore, an initial logical place to search for neural mechanisms of negative symptoms is in the frontal lobes.

Positive symptoms, on the other hand, represent distorted functions. Hallucinations are abnormal perceptions, and usually they represent abnormal auditory perceptions. A variety of mechanisms could be postulated, including abnormal neuronal activity in the auditory cortex, the temporal association cortex, or memories encoded in temporo-limbic regions such as the amygdala or hippocampus (Andreasen, 1986). Mechanisms for other positive symptoms, such as delusions, disorganised speech, or bizarre behaviour, are more difficult to localise. Since delusions reflect an abnormality in inference and judgement, their mechanisms are probably relatively complex and could arise from a generalised increase in arousal, a phenomenon that could be mediated by a variety of neurochemical mechanisms and brain systems. Disorganised speech and bizarre behaviour probably reflect similar mechanisms.

Structural imaging studies

The development of the techniques of brain imaging have given us a variety of méthods in order to explore possible neural mechanisms that may underly positive or negative symptoms. Structural imaging techniques, particularly computed tomography (CT), were among the earliest to be applied to the study of schizophrenia (see also Crow, this volume). Although earlier pathological and pneumoencephalographic techniques had been applied in order to evaluate structural abnormalities in schizophrenia, CT offered the great advantage of applicability to large samples of patients and to normal controls.

In the first CT study, published in *Lancet*, in 1976, Johnstone *et al.* reported that patients suffering from schizophrenia tended to have a significantly greater degree of ventricular enlargement than did a matched control group. This study was initially greeted with criticism and scepticism because the patients studied were relatively old, chronically institutionalised, and even included some who had been treated with leucotomy. Replications were reported during the next few years, however, and now enlargement in the ventricular system has become one of the most widely replicated findings in psychiatry (Weinberger *et al*, 1979*a*, *b*; Andreasen *et al*, 1982; Jaskiw *et al*, 1987).

The initial Johnstone *et al* study also reported an association between ventricular enlargement, negative symptoms, and cognitive impairment. Other studies have sought for such relationships, and they have been found in some, but not all. The most consistent correlate of ventricular enlargement appears to be cognitive impairment, and indicators of poor premorbid functioning such as unemployment, lower educational status and poor premorbid adjustment have also been confirmed in a relatively large number of studies (Johnson *et al*, 1976; Rieder *et al*, 1979; Weinberger *et al*, 1980*a*, *b*; Andreasen *et al*, 1982; Pearlson *et al*, 1984, 1985). Negative symptoms have also been shown to be associated with a poor response to treatment. Thus, CT studies have provided some partial confirmation of the two syndrome hypothesis, but a recent report from the Northwick Park group (Owens *et al*, 1985) is considerably more negative than the initial report in *Lancet*.

The relationship between the type of brain abnormality involved and the various clinical correlates remains obscure. Ventricular enlargement has been the finding most consistently observed. Some studies have described cortical atrophy as well, while a few also report cerebellar atrophy. Ventricular enlargement without cortical atrophy is also quite common, however. A strong association between cortical atrophy and ventricular enlargement would suggest a mechanism involving diffuse neuronal loss. The frequent dissociation of these two abnormalities suggests, however, that for many patients suffering from schizophrenia the atrophy might be selective and possibly even limited to grey matter nuclei surrounding the ventricles, such as the caudate, putamen and thalamus. Alternately, white matter fibres running through this area could be involved.

Magnetic resonance imaging (MRI) has also recently been applied to the study of structural abnormalities in schizophrenia. MRI has a number of advantages over CT scanning because it permits the brain to be sectioned in multiple planes and has excellent grey-white resolution. Therefore it can be used to conduct detailed morphometric studies involving the size of specific structures potentially relevant to schizophrenia, such as the frontal lobes, the hippocampus, amygdala, basal ganglia, and corpus callosum. An initial study using MRI in schizophrenia reported a decrease in frontal lobe size in schizophrenic patients; in addition, decreased cerebral and cranial size were observed and appeared to be secondary to the decrease in frontal size (Andreasen *et al*, 1986). This study suggested that the abnormality occuring in schizophrenia might be due to some early developmental mechanism, since cranial growth occurs in harmony with cerebral growth and is largely completed during the first two years of life.

This finding has not been confirmed in a second study, however, perhaps because patients and controls are more closely matched in the second study (Andreasen *et al*, in press). The controls in the first study were educationally and socio-economically advantaged as compared to the schizophrenics, which might partially account for the highly significant differences in brain measures that were observed. In this initial study, decreased cranial and cerebral size were also noted to be related to negative symptoms and cognitive impairment, but no relationship with frontal lobe size was observed.

Thus the structural imaging studies indicate some relationship between negative symptoms and cerebral abnormalities, but the results are neither consistent nor overwhelming. The failure to find strong consistent relationships between negative symptoms and indicators of cerebral abnormality may reflect the lack of any relationship, or alternatively it may reflect the inherent crudeness of the measures involved. At the clinical level, secondary negative symptoms may produce the major confounder, as may the effects of neuroleptic drugs. At the neural level, CT and MRI may not be sufficiently sharp instruments in order to disect and identify the role of brain structure in producing negative symptoms.

Functional imaging techniques

Functional imaging techniques, which involve the measurement of regional cerebral blood flow with cortical probes or with single photon emission computed tomography (SPECT) and positron emission tomography (PET), offer an alternative and perhaps more powerful approach to understanding the neural mechanisms that underlie the phenomenology of schizophrenia.

The earliest reports of functional abnormalities in schizophrenia were presented by Ingvar & Franzen (1974), who used measurements of regional cerebral blood flow in order to identify abnormalities in perfusion in the frontal lobes. This abnormality was considered to represent the decreased level of metabolic activity sometimes referred to as 'hypofrontality'. Their studies have been replicated by some investigators, but not by all (Matthew *et al*, 1982; Ariel *et al*, 1983; Gur *et al*, 1985). Buchsbaum *et al* (1982, 1985, 1987) have also identified hypofrontality using PET scanning, although this too has not been consistently replicated (Sheppard *et al*, 1983; Widen *et al*, 1983). Functional studies have been conducted with increasing methodological sophistication, and more recently, they have involved the use of cognitive challenges in order to determine whether patients with schizophrenia have difficulty in activating specific brain regions. These techniques have been applied primarily to the frontal system, using tests such as the Wisconsin Card Sorting test or the Continuous Performance test (Weinberger *et al*, 1986; Berman *et al*, 1986; Buchsbaum & Haier, 1987). These studies have indicated that patients with schizophrenia do have difficulty in activating their frontal lobes in response to a cognitive challenge and therefore are consistent with the general hypothesis of frontal lobe dysfunction in schizophrenia. None of these studies has attempted to relate hypofrontality specifically to negative symptoms, however.

An interesting recent complementary finding with PET has involved a relative increase in metabolic activity in subcortical regions in schizophrenia, particularly the basal ganglia (Gur *et al*, 1987; Early *et al*, 1987). This pattern of increased activity in subcortical regions in schizophrenia, especially when coupled with hypofrontality, may suggest a model that could account for the simultaneous generation of positive and negative symptoms. Such a model was proposed in 1983 by Bannon & Roth. Their model can explain the mixture of positive and negative symptoms in schizophrenia and evidence of both increases and decreases in dopamine function. Based on animal studies that indicate that selective prefrontal cortical dopamine lesions enhance subcortical dopamine transmission, they postulated that patients with schizophrenia may simultaneously have hypodopaminergic function in their prefrontal cortex and hyperdopaminergic activity in subcortical or limbic regions. The hypofrontal activity could express itself as the classic negative symptoms of schizophrenia, while the increased subcortical limbic activity would be reflected in movement abnormality or positive symptoms such as hallucinations. This combination of symptoms could be explained by reduced prefrontal cortical dopamine, leading to relative activation of other dopamine systems in the basal ganglia or limbic regions that would normally be modulated by feedback loops from the prefrontal cortex. This model is consistent with a number of reports in the literature. For example, there is some suggestion that patients with schizophrenia may have decreased homovanillic acid (a dopamine breakdown product), which may be correlated with indices of cerebral atrophy such as ventricular enlargement and with negative symptoms, implying that some manifestations of schizophrenia actually reflect hypodopaminergic activity (Van Kammen *et al*, 1983; Meltzer, 1987). Low doses of neuroleptic drugs have been reported to be more efficacious in treating negative symptoms and to exert their functional effect through enhancing dopamine transmission (Lecrubier *et al*, 1980; Mackay, 1980).

There are many lines of evidence that suggest a relationship between hyperdopaminergic activity and positive symptoms. It has been consistently shown that neuroleptic drugs produce dopamine-2 (D2) receptor blockade and that the reduction in positive symptoms is related to the degree of receptor blockage. On the other hand, amphetamine-like compounds act as dopamine agonists and produce positive symptoms (Randrup & Munkvard, 1965; Creese *et al*, 1976; Seeman *et al*, 1976; Snyder, 1976). An increased number of D2 receptors has been reported in the basal ganglia and nucleus accumbens in a substantial series of postmortem studies (Owen *et al*, 1978; Kleinman *et al*, 1982; Weinberger *et al*, 1983; Seeman *et al*, 1984).

Functional imaging techniques also provide an opportunity for measuring dopamine activity *in vivo*, since methods have recently been developed for quantitatively measuring D2 receptor density in the human brain (Sedvall *et al*, 1986; Wong *et al*, 1986*a*, *b*). If D2 receptors are indeed increased in subcortical regions and this represents an important mechanism producing positive symptoms, then PET scanning provides a powerful tool for testing the above hypothesis concerning the interrelationships between positive and negative symptoms, imbalances in frontal v. subcortical regions, and imbalances in dopamine activity. Unfortunately, the results of these studies are not conclusive either. Wong *et al* (1986*c*) have reported increased D2 receptor density in the caudate in schizophrenia, but a report from Farde *et al* (1987) indicates that the Karolinska group has been unable to confirm this finding. Both these studies have examined drug naive (i.e. never medicated) schizophrenic patients, which is an ideal sample in order to determine whether a relative increase in D2 receptor density occurs in schizophrenia.

Conclusion

As the above review indicates, the neural mechanisms that may explain positive or negative symptoms have not yet been determined. The initial model proposed by Crow, which contrasts a negative syndrome characterised by structural abnormalities with a positive syndrome characterised by neurochemical abnormalities, is probably too simple, since it cannot account for mixtures of positive and negative symptoms or changes in phenomenology over time. This hypothesis had great heuristic value, for it led to an interest in understanding the symptoms of schizophrenia in terms of neural mechanisms. More complex models must be developed that continue to build on our growing knowledge concerning normal brain structure and function, the complex interactions of neural circuits connecting various brain regions, and the mechanism of the action of neuroleptic drugs.

Figure 1 illustrates one such model, which attempts to integrate the knowledge that can be gleaned to date from the various structural and functional imaging studies just described, as well as our existing knowledge concerning the interrelationships between neurochemical systems and neural circuits. This model attempts to account for both the cross-sectional and longitudinal interrelationships between positive and negative symptoms. It suggests that in the normal brain frontal

Normal	Frontal	⇌	Subcortical–limbic	No symptoms
Early psychosis	Frontal	⇌	**Subcortical–limbic**	Positive symptoms
Florid severe psychosis	~~Frontal~~	⇌	**Subcortical–limbic**	Positive and negative symptoms
Endstage psychosis	~~Frontal~~	⇌	~~**Subcortical–limbic**~~	Negative symptoms

FIG. 1 Model for neural mechanisms.

and subcortical systems remain in balance, and no symptoms of any type occur. Early in the course of psychosis, this system falls into imbalance with a relative hyperactivity in subcortical regions (either limbic or basal ganglia); this functional hyperactivity expresses itself in prominent positive symptoms. As these symptoms persist, the hyperactive subcortical regions produce excessive stimulation to the frontal lobes, which in turn respond by down-regulating. In this instance, patients have a mixture of positive and negative symptoms, reflecting the relative hypoactivity of the frontal lobes and the hyperactivity of subcortical regions. Finally, in end-stage psychosis, the limbic system down-regulates as well, leaving the patient with the most typical long-term picture, prominent negative symptoms in the absence of positive symptoms, frequently referred to as the 'defect state' or 'burned out schizophrenia'.

While this model has heuristic value in that it provides a more complex and dynamic description of the phenomenology and neurobiology of schizophrenia, it too is almost certainly an oversimplification. It is presented as an attempt to integrate our existing knowledge and to suggest future directions that should be explored in schizophrenia research. These directions will stress the use of *in vivo* imaging techniques, the careful integration of clinical description and evaluation of neural mechanisms, a recognition of the structural and neurochemical complexity of the human brain and the importance of studying patients longitudinally and explaining the course of the illness through dynamic rather than static models.

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Negative Symptoms, Tardive Dyskinesia and Depression in Chronic Schizophrenia

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The existence of a definable and distinct negative syndrome within schizophrenia remains to be established (Barnes & Liddle, 1989). Addressing this issue, Sommers (1985) discusses three stages required to demonstrate validity for a syndrome. These are first, that the signs and symptoms must be shown to occur together. Second, operational definitions must be developed which will reliably identify and rate and features, and third, the relationships between the syndrome and other variables must be shown to be predictable. With respect to the second and third stages, this paper reports briefly on two recent studies which explored the relationship between negative features and other clinical features, specifically depressive symptoms and drug-induced movement disorder. The results of such studies (see also McKenna *et al*; and Lindenmayer & Kay, this volume) allow some assessment of the ability of the rating methods used to discriminate between negative symptoms and features such as drug-related bradykinesia and depressive features.

The first investigation examined the relationship between negative symptoms, parkinsonism and depressive features in a population of chronic schizophrenic in-patients (Barnes *et al*, 1989). The second study looked at the relationship between tardive dyskinesia and negative symptoms in another sample of similar patients.

A study of depression, parkinsonism and negative symptoms in chronic schizophrenic in-patients

Background

A variety of aetiological theories have been proposed to explain the relatively common occurrence of depression in schizophrenic patients. McGlashan & Carpenter (1976*b*) have used the term 'post-psychotic depression' which implies that the symptoms occur during recovery from a psychotic episode, and constitute the patient's response to their recent ordeal. Knights & Hirsch (1981) found that depressive features identified during relapse tended to decrease in severity with effective anti-psychotic drug therapy, in parallel with the psychotic phenomena. They suggested, therefore, that the depression may be 'revealed' as the more florid symptoms subside with treatment.

Other authors have assumed a direct causal role for anti-psychotic drugs, referring to 'pharmacogenic depression' (Ananth & Ghadirian, 1980; Galdi, 1983). Indirectly, anti-psychotic drugs can induce parkinsonism, which may present with symptoms such as bradykinesia and loss of spontaneity which mimic a retarded depressive syndrome, so-called 'akinetic depression' (Rifkin *et al*, 1975; Van Putten & May, 1978). However, these features, and other parkinsonian symptoms such as lack of facial expression could also confound the assessment of negative symptoms, particularly affective flattening.

Furthermore, the association between depressive features and certain 'negative' schizophrenic symptoms, such as anhedonia, anergia, feelings of emptiness and emotional withdrawal (McGlashan & Carpenter, 1976*b*; Roth, 1970; Stern *et al*, 1972) remains unclear. For example, features such as anhedonia, social withdrawal and poverty of speech which are included in some rating scales for negative symptoms are also recognised features of depression.

Exploring this area, Craig *et al* (1985) found an association between parkinsonian symptoms and depressive features in a group of schizophrenic in-patients. In a sample of schizophrenic out-patients, Prosser *et al* (1987) reported a significant correlation between scores on the Brief Psychiatric Rating Scale (BPRS) negative symptom subscale, comprising items from emotional withdrawal, motor retardation and blunted affect, and both severe parkinsonism and vegetative features of depression.

One aim of this study was to examine the possible overlap between the clinical assessment of negative symptoms, depression and drug-induced parkinsonism in a population of chronic schizophrenic patients. A refined assessment of negative symptoms and depression was attempted in a population of chronic schizophrenic in-patients.

Method

All 287 patients on the 11 non-geriatric long-stay wards of Horton Hospital, Epsom were screened; 239 carried a clinical diagnosis of schizophrenia, and of these 222 fulfilled DSM–III criteria for schizophrenia.

Item 23 of the Present State Examination (PSE) (Wing *et al*, 1974) which rates depressed mood, was used to screen the population, and those patients with this core feature of depression were identified. Rating on PSE item 23 and a full Comprehensive Psychopathological Rating Scale (CPRS) (Asberg *et al*, 1978) was achieved in 194 patients. The failure to complete the assessment interview in the remaining 28 cases was for a variety of reasons, the most common being mutism (12 cases), persistent refusal to co-oprate (5) and poor command of English (4). These assessments were carried out by a pair of raters (DAC and MP).

Depressed mood was rated as present in 25 patients, that is they received a score of 1 or 2 for PSE item 23. This represented a point prevalence of 13% for this symptom within the population. These 'depressed' patients were matched for age, length of illness and sex with a group of 'control' patients scoring zero on PSE item 23.

Within one week of assessment, the two matched groups were blindly assessed by a second pair of investigators (TREB and PFL) using the Scale for Assessment of Negative Symptoms, SANS (Andreasen, 1982; see also Andreasen, this volume), the Beck Inventory (Beck *et al*, 1961), the Extrapyramidal Rating Scale (EPRS) (Simpson & Angus, 1970), and a rating scale for tardive dyskinesia (Barnes & Trauer, 1982).

The matched pairs of initially 'depressed' patients and their controls were then reassessed 3 months later using the same rating instruments and procedure. Details of each patient's medication were recorded and anti-psychotic drug dose converted to chlorpromazine equivalents per day.

Results and discussion

To examine the correlation between PSE depressed mood and other variables, the Montgomery-Asberg depression scale, the MADRS (Montgomery & Asberg, 1979), was used. This is a depression rating scale of 10 items derived from the full CPRS. The items are: sadness; inner tension; inability to feel; pessimistic thoughts; lassitude; concentration difficulties; reduced appetite; reduced sleep; suicidal ideas; and apparent sadness on observation.

For this analysis, two subscores for negative symptoms were derived from the SANS. Affective flattening (AF) was the total of the scores for six items: unchanging facial expression; decreased spontaneous movements; poverty of expressive gestures; poor eye contact; affective non-responsivity; and lack of vocal inflection. Alogia (AL) was derived similarly from the scores for four items in this section of the SANS: poverty of speech; poverty of content of speech; blocking; and increased latency of response.

A score for positive symptoms was derived from the CPRS, being a total of the scores for the following items: feeling controlled; disrupted thoughts; ideas of persecution; ideas of grandeur; other delusions; commenting voices; other auditory hallucinations; visual hallucinations; and other hallucinations.

Comparison of the PSE 'depressed' group with the control group at initial assessment revealed a significantly higher mean MADRS score in the former (see Table I). The Beck depression scores also showed a highly significant difference between the PSE depressed and control groups at initial assessment. This suggests that those patients identified on the basis of depressed mood had other features of depression conforming to a depressive syndrome.

This tentative conclusion was supported to some degree by the results of a 3-month follow-up assessment. By the end of this period, ten of the originally depressed patients were no longer rated as having depressed mood, and five of the matched controls had developed

TABLE I

Comparison between chronic schizophrenic patients with depressed mood (PSE item 23) and group without depressed mood, matched by sex, age and length of illness

	'Depressed' (n = 25)	*Controls* (n = 25)	*Significance of difference*
Mean MADRS score	15.9 (SD 8.1)	3.44 (SD 4.6)	$P < 0.001$
Mean Beck score	19.5 (SD 10.9)	10.2 (SD 9.2)	$P = 0.004$
Mean AF score	11.4 (SD 7.3)	9.1 (SD 5.7)	NS
Mean AL score	3.0 (SD 2.2)	1.96 (SD 1.5)	NS
Mean parkinsonism score	0.8 (SD 0.9)	0.68 (SD 0.9)	NS
Oro-facial tardive dyskinesia present	16 (64%)	17 (68%)	NS
Mean daily anti-psychotic drug dose[1]	655 (SD 119)	991 (SD 355)	NS

[1] Calculated as chlorpromazine equivalents, mg/day (Davis, 1976; Baldessarini, 1978).

depressed mood. The MADRS and Beck scores co-varied closely with the presence or absence of depressed mood, and had increased significantly in those control patients who had developed depressed mood. There was no significant difference between the initial depressed and non-depressed groups on the SANS affective flattening score suggesting that depression and affective flattening are distinct clinical syndromes. This finding supports that of Presser *et al* (1987) who found no association between negative symptoms and 'cognitive' features of depression. However, there was a trend at the near 5% level for the SANS alogia score to be higher in the depressed group. This may reflect that poverty of speech and increased latency of response, which are included in the alogia score, are recognised features of depression.

There were no significant differences between the depressed and non-depressed groups on scores for parkinsonism. This result suggests that akinetic depression was not a major factor in the genesis of depressive features in this sample. Further, there was no significant difference in regard to dosage of anti-psychotic medication calculated in chlorpromazine equivalents in mg/day. This finding fails to support the idea of depression as a direct effect of drug treatment.

In conclusion, therefore, depression in this sample of long-stay, chronic schizophrenic in-patients was fairly common, conformed to a typical depressive syndrome as measured by the MADRS and the Beck Depression Inventory in most patients, and was distinct from affective flattening as rated on SANS items. However, some overlap between depression and SANS items such as poverty of speech and increased latency of response seemed to be present. The depressive syndrome identified was unrelated to factors which would support the hypotheses of 'pharmacogenic' or 'akinetic' depression. Whether this apparently typical, but sometimes transient depressive syndrome in chronic patients is an integral part of schizophrenia, or whether it reflects episodes of depression related to their adverse circumstances and multiple handicaps remains a matter of speculation.

A study of negative symptoms and tardive dyskinesia in schizophrenia

Background

The second study was essentially a survey of chronic schizophrenic in-patients, one aim of which was to examine the relationship between movement disorder and negative symptoms in such cases. An association with certain negative symptoms has been found for both schizophrenic abnormal movements and what are usually considered to be drug-related abnormal movements, that is to say, tardive dyskinesia.

Discussing first the clinical associations of movements related to the schizophrenic illness, Yarden & Discipio (1971) reported on a sample of young, drug-free schizophrenic patients presenting with a variety of abnormal movements, labelled as choreiform and athetoid, and including tics, stereotypies, and mannerisms. Their follow-up data, after 2½ to 3½ years, led them to conclude that schizophrenic patients distinguished by abnormal movements constituted a group with an early onset, a steadily progressive course, severe deterioration with marked thought disorder and a resistance to pharmacological treatment. In line with this report, recent studies by Manschrek and co-workers (Manschrek *et al* 1982; Manschrek & Ames, 1984) have found that disturbed voluntary motor activity, which they claimed was unrelated to drug-effects, occurred frequently among schizophrenic patients. They reported statistically significant associations between this apparently schizophrenic movement disturbance and neurological 'soft' signs, cognitive impairment, affective blunting and formal thought disorder. One conclusion would be that schizophrenic patients with negative symptoms of the Type II syndrome are more likely to exhibit motor abnormalities, independent of drug treatment.

Similarly, tardive dyskinesia has been found to be more common in patients with negative features in the majority of studies which have examined this issue (Barnes & Liddle, 1985; Waddington, 1987). Studies comparing dyskinetic and non-dyskinetic schizophrenic patients have consistently reported a significant association between tardive dyskinesia and symptoms such as emotional withdrawal, blunted affect, poverty of speech, motor retardation and reduced social interest. Those studies which have failed to find this association have tended to involve younger patients.

The present study investigated this association further, using rating scales designed to refine the assessment of negative symptoms in schizophrenia, and measures of movement disorder which attempted to discriminate between dyskinesia such as choreiform and dystonic movements and other abnormal movements such as restlessness associated with akathisia, stereotypies and mannerisms.

Method

The study population comprised all 56 patients on three long-stay psychiatric wards who satisfied DSM—III criteria for schizophrenia. Rating scales for tardive dyskinesia (Barnes & Trauer, 1982) and akathisia (Barnes, 1989) were administered by an investigator (PFL) who was blind to the ratings for negative symptoms. The SANS and the Manchester Scale

(Krawiecka *et al*, 1977; see also Hyde, this volume) were administered by another investigator (TREB) blind to the movement ratings.

Results and discussion

Applying the criterion level of symptomatology on the rating scale for tardive dyskinesia yielded 37 patients with oro-facial dyskinesia and 20 without. Those with dyskinesia were, predictably, significantly older. Comparing the two groups, those with dyskinesia were apparently receiving significantly less anti-psychotic drug, a finding also reported by Opler *et al* (1984) and Waddington & Youssef (1986). However, this association between oro-facial dyskinesia and dose of anti-psychotic drug was not significant when the partial correlation, taking age into account was calculated.

A number of significant correlations between oro-facial dyskinesia score and negative symptoms were found (see Table II). However, a further analysis, taking age into account, was indicated. But, a partial correlation was not statistically appropriate because a linear relationship between tardive dyskinesia and age could not be assumed. For example, in previous studies (Kidger *et al*, 1980; Barnes *et al*, 1983) we had examined the association between age and oro-facial dyskinesia. In psychiatric patients receiving anti-psychotic medication the amount of oro-facial dyskinesia showed the most marked increase in the sixth decade, while drug-naive, normal individuals tended to develop spontaneous oro-facial dyskinesia some 15 years later.

TABLE II

Significant correlations between oro-facial dyskinesia and negative symptoms of schizophrenia

	Correlation	
	r	*P*
Manchester Scale items		
Poverty of speech	0.42	0.001
Psychomotor retardation	0.35	0.004
Flatness of affect	0.24	0.04
SANS subscores		
Alogia	0.48	<0.001
Affective flattening	0.30	0.02

Therefore, to explore the relationship between negative symptoms, tardive dyskinesia and age in this present study we examined the closeness of fit of our data to an age-threshold model, using a curve-fitting statistical technique. This model assumed a low prevalence of tardive dyskinesia in young patients and a high prevalence in elderly patients, and that tardive dyskinesia is likely to emerge during mid-life. We attempted to demonstrate that our data were consistent with this model, and further, to determine the age range within which tardive dyskinesia developed in two groups, those patients with negative symptoms and those without. The presence of negative symptoms was determined by a total score of 2 or more for the combined ratings for the poverty of speech and flattened affect items of the Krawiecka scale.

The best fit of the model for age of onset of tardive dyskinesia in patients with negative symptoms was 46 years old with a standard deviation of 8 years, while for patients without negative symptoms the age of onset figure was 59 years with a standard deviation of the threshold of 10 years. Thus, there is a difference of 13 years between the ages of onset for these two groups. This finding suggests that the schizophrenic patients with negative symptoms developed tardive dyskinesia significantly earlier than those patients without such symptoms, that is, they are more susceptible to the condition. If negative symptoms are an indication of vulnerability to tardive dyskinesia this would be in line with the hypothesis that negative symptoms and abnormal movements share elements of underlying pathology (Jeste *et al*, 1984; Barnes & Liddle, 1985).

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Negative Symptoms: Relationship to Other Schizophrenic Symptom Classes

P.J. McKENNA, C.E. LUND and A.M. MORTIMER

If negative symptoms represent a distinct class of schizophrenic symptoms, they should, to paraphrase Bleuler (1911), be more closely related to each other than they are to other schizophrenic symptoms. The first part of this statement, that negative symptoms are intrinsically related to each other, has received considerable experimental support (Andreasen, this volume; Mortimer *et al*, this volume). The second, that negative symptoms are unrelated to other schizophrenic symptoms, has been somewhat more unevenly investigated.

Several studies have examined the occurrence of negative symptoms in relation to the productive, florid or 'positive' symptoms of schizophrenia (e.g. Owens & Johnstone, 1980; Andreasen & Olsen, 1982; Lewine *et al*, 1983; Kay *et al*, 1986; Kulhara *et al*, 1986). These all found insignificant or even inverse correlations between the presence of positive and negative symptoms, but they are all open to methodological criticisms. For instance, the measures of negative symptoms were sometimes crude, and positive and negative symptoms were invariably not rated independently of each other. In addition, there is uncertainty over which symptoms should be considered positive. While delusions and hallucinations have, by consensus, always been considered positive, formal thought disorder has been considered at different times both positive (e.g. Crow, 1980; Andreasen, 1982) and negative (Wing & Brown, 1970; see also Wing, this volume; Liddle *et al*, this volume). The status of catatonic phenomena within the positive:negative framework has so far received little consideration.

The independence of negative symptoms from the depressive states which may complicate schizophrenia (Hirsch, 1982; Johnson, 1986) is another area of crucial theoretical importance to the construct of negative symptoms. There are equally obvious practical implications of this issue, particularly with regard to the reliability and validity of measurement of negative symptoms. However, investigaton of the distinction of those two syndromes has so far been slight (Lewine *et al*, 1983; Prosser *et al*, 1987).

Finally, the concept of negative symptoms refers to a constellation of deficits in schizophrenia; but they are by no means the only deficits seen in the disorder. It seems established beyond reasonable doubt that some schizophrenic patients show wide-ranging dementia-like cognitive impairments (Payne, 1973; Crow & Stevens, 1978). An association of negative symptoms and cognitive impairment in schizophrenia has been found in some studies (Owens & Johnstone, 1980; Andreasen & Olsen, 1982; Kay *et al*, 1986). More recent work, on the other hand, has suggested that cognitive impairment shows a more complex pattern of affiliation (Bilder *et al*, 1985; Robertson & Taylor, 1985; Liddle, 1987).

Study I

In the first of two studies reported here, the relationship of negative symptoms to positive symptoms and depression in schizophrenia was examined systematically, and under blind conditions.

Method

The sample consisted of 62 patients drawn from acute, rehabilitation and long-stay services of two hospitals, and encompassing all grades of severity and chronicity. All patients met DSM–III criteria for schizophrenia except for a small number who did not clearly fulfil the criterion of deterioration; these all met Research Diagnostic Criteria. Ages ranged from 20 to 72; all were of normal premobid intelligence and had no history of drug or alcohol abuse. All patients were taking neuroleptic medication and, in order to minimise masking of negative symptoms by florid exacerbations of psychosis, were rated when they had been relatively stable for at least 2 months.

One interviewer rated negative symptoms using the High Royds Evaluation of Negativity (HEN) scale (Mortimer *et al*, this volume) and the Scale for the Assessments of Negative Symptoms (SANS) (Andreasen, 1982). A second interviewer blind to this information, then completed the Comprehensive Psychopathology Rating Scale (CPRS) (Asberg *et al*, 1978) a 65-item inventory covering all aspects of psychiatric sympomatology, and the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery & Asberg, 1979) observer rated scale for depression. Those patients who were capable completed the self-rated Hospital Anxiety and Depression Scale (HAD) (Zigmond & Snaith, 1983) questionnaire for depression and anxiety.

Three measures of positive symptoms were derived from the CPRS: CPOS (*narrow*) consisted of summed scores on nine delusion and hallucination items; CPOS (*intermediate*) comprised these plus six further items encompassing other abnormal ideas, first-rank symptoms and formal thought disorder; CPOS (*broad*) consisted of these plus six other items describing non-neurotic, non-affective symptoms (e.g. derealisation, agitation, mannerisms and postures) which might reasonably be considered to accompany acute exacerbations of schizophrenia. Depression was measured as the total score on the MADRS and on the depression subscale of the HAD.

Results

Individual scores were correlated using Spearman's non-parametric method. Neither HEN nor SANS summary scores showed any significant correlation with positive symptoms, however these were defined. (See Table I).

TABLE I

Correlations between negative and positive symptoms

	CPOS (narrow)	*CPOS (intermediate)*	*CPOS (broad)*
HEN summary score	0.10 (NS)	0.08 (NS)	0.05 (NS)
SANS summary score	0.08 (NS)	0.09 (NS)	0.06 (NS)

HEN summary scores showed no significant correlation with either measure of depression. On the other hand, SANS summary scores showed a modest correlation with MADRS scores ($r = 0.29$; $P = 0.03$) and a stronger correlation with the depression scale of the HAD ($r = 0.41$; $P = 0.006$) (see Table II).

TABLE II

Correlation between negative symptoms and depression

	MADRS	*HAD (D)*
HEN summary score	0.03 (NS)	0.12 (NS)
SANS summary score	0.30 ($P = 0.03$)	0.41 ($P = 0.006$)

Study II

The principal aim of this study was to examine the relationship of negative symptoms to formal thought disorder, motor disorder and cognitive impairment. It was also desired to explore possible interactions of factors like severity and chronicity of illness, which might be important determinants of the expression of some symptoms.

Method

Using the HEN and the SANS 77 schizophrenic patients demographically similar to those in Study I and meeting the same criteria were rated. This rater also completed part of the CPRS, in order to allow ratings of CPOS (*narrow*) to be made. A second interviewer, blind to this information, rated formal thought disorder using the positive formal thought disorder and alogia scales in the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen, 1979; Andreasen, unpublished), and cognitive impairment using the Mini-Mental Status (MMS) (Folstein *et al*, 1975). Ratings of motor disorder were also made by this interviewer using the scale developed by Rogers (1985). This allows a detailed, non-prejudicial, evaluation of all clinically observable motor disorders, from extrapyamidal symptoms to catatonic phenomena. The scale allows extraction of subscores for productive phenomena (i.e. those distinguished by their presence) and deficit phenomena (i.e. those distinguished by the absence/diminution of a normal function).

Severity of illness was measured using the scale of Endicott *et al* (1976), and chronicity was taken as the average number of years between maximum (first discernible psychotic symptoms) and minimum (first psychotic admission to hospital) durations.

Results

Both HEN and SANS summary scores showed highly significant associations with both severity ($r = 0.72$ and 0.63; $P < 0.001$) and chronicity ($r = 0.54$ and 0.43; $P < 0.001$).

Correlations between negative symptoms, positive symptoms, and formal thought disorder are summarised in Table III. Both HEN and SANS summary scores showed no significant correlations with CASH positive formal thought disorder, but highly significant correlations with CASH alogia. Positive symptoms showed an exactly inverse pattern of correlations with these items. Both positive formal thought disorder and alogia were significantly correlated with severity ($r = 0.39$; $P = 0.001$ and $r = 0.25$; $P = 0.02$), but not with chronicity ($r = 0.14$ and 0.14 NS), controlling for these made no difference to the significance of the correlations.

HEN and SANS scores were highly significantly correlated with total motor disorder scores on the Rogers scale. This remained true on division into productive and deficit subscores. However, motor disorder was highly significantly correlated with both severity ($r = 0.64$; $P < 0.001$) and chronicity ($r = 0.44$; $P < 0.001$). As both HEN and SANS total scores were

TABLE III

Correlations between negative symptoms and formal thought disorder

	Positive FTD	*Alogia*
HEN summary score	0.16 (NS)	0.61 ($P < 0.001$)
SANS summary score	0.11 (NS)	0.58 ($P < 0.001$)
CPOS (narrow)	0.41 ($P < 0.001$)	0.03 (NS)

also correlated with these variables (see above) it was possible that the true correlations between negative symptoms and motor disorder were being masked by their mutual association with severity and chronicity. In fact, when severity and chronicity were controlled for, the partial correlations between HEN and SANS scores and Rogers total score were reduced to marginal significance; there were no longer any significant correlations with productive motor disorder; there were, however, highly significant correlatons with deficit motor scores. (See Table IV).

MMS total score showed significant inverse correlations with HEN and SANS scores ($r = -0.63$ and -0.58; $P = 0.001$); there was no correlation with CPOS (*narrow*) ($r = 0.13$; NS). In addition MMS showed significant correlations with both positive formal thought disorder ($r = -0.35$; $P = 0.004$), 'alogia' ($r = -0.22$; $P = 0.05$), and Rogers total scores ($r = -0.56$; $P = 0.001$). Controlling for severity and chronicity resulted in a marked weakening in the correlation of MMS score and HEN summary score ($r = -0.31$; $P = 0.03$) and the virtual disappearance of this with the SANS ($r = -0.16$; $P = 0.17$). The relationships with CPOS (*narrow*) positive formal thought disorder, alogia and motor disorder remained essentially unchanged.

Discussion

The two studies reported here add further documentation to the findings of several previous studies (Owens & Johnstone, 1980; Andreasen & Olsen, 1982; Lewine *et al*, 1983; Rosen *et al*, 1984; Pogue-Geile and Harrow, 1985; Kay *et al*, 1986; Kulhara *et al*, 1986), that occurrence of negative symptoms is uncorrelated, or even inversely correlated with that of positive symptoms. The validity of the positive:negative dichotomy in schizophrenia appears to be established beyond any reasonable doubt, though it may remain something of an oversimplification.

The present study and Barnes *et al* (this volume) also strengthen previous findings (Lewine *et al*, 1983; Prosser *et al*, 1987) that negative symptoms are separable from depression in schizophrenia. In our study there was no significant correlation between HEN scores and two indices of depression. The significant associations between SANS scores and both these measures could argue against such a conclusion, but might alternatively reflect a 'contamination' of the SANS scale by depression items: the SANS includes a section devoted to anhedonia, plus items to be rated subjectively by the patient, both of which might plausibly measure depressive symptoms. Taken as a whole, the available evidence suggests that negative symptoms and depression in schizophrenia are two largely independent domains of pathology.

The results of our second study, in particular, provide the first evidence that the concept of productive and deficit in schizophrenia extends considerably beyond the traditionally defined positive and negative symptom clusters. Thus, Andreasen's positive formal thought disorder clearly emerged as positive, and alogia as negative symptoms on statistical grounds. Motor disorder initially showed a significant association with negative symptoms (Andreasen & Olsen, 1982; Manschreck *et al*, 1982), but this appeared to be an artefact of their mutual association with severity and chronicity of illness. When severity and chronicity were controlled for, a striking pattern of correlation between negative symptoms and deficit, but not productive motor disorder emerged. A parallel, but somewhat more complex pattern of correlations between positive symptoms and productive but not deficit motor disorder was also seen. This and further findings will be described in full in a subsequent communication (Mortimer *et al*, 1990).

TABLE IV
Correlations between negative symptoms and motor disorder

	Rogers total	*Rogers productive*	*Rogers deficit*
HEN summary score	0.70 (P 0.001)	0.54 ($P < 0.001$)	0.62 ($P < 0.001$)
SANS summary score	0.63 (*P 0.001*)	*0.44* ($P < 0.001$)	0.62 ($P < 0.001$)
	Controlling for severity and chronicity		
HEN summary score	0.26 (P 0.056)	−0.07 (NS)	0.56 ($P < 0.001$)
SANS summary score	0.14 (NS)	−0.15 (NS)	0.55 ($P < 0.001$)

The findings relating to cognitive impairment, however, remain difficult to accommodate within the positive:negative framework. Several studies (e.g. Owens & Johnstone, 1980; Andreasen & Olsen, 1982; Kay *et al*, 1986) have found highly significant associations between negative symptoms and cognitive impairment, as might be anticipated on the basis that they are both deficits. However, in our study there were additional significant associations with formal thought disorder (of both productive and deficit types) and motor disorder. Controlling for severity and chronicity, in fact, weakened the particular association with negative symptoms to the point of equivocality. It seems clear that an association with negative symptoms is only one aspect of a broader and ill-understood pattern of affiliations of cognitive impairment in schizophrenia, a conclusion also reached by other authors (Bilder *et al*, 1985; Robertson & Taylor, 1985; Liddle, 1987).

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Depression, Affect and Negative Symptoms in Schizophrenia

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The relationship of depression with affect deficit in schizophrenic patients continues to challenge both the clinician and the researcher. Often there is considerable difficulty in differentiating these two affect states in a reliable and valid fashion. On the observational level, depressed affect often appears somewhat restricted, having lost the full range of the euthymic state. On a subjective level, schizophrenic patients often complain of anhedonia, a defect in pleasure capacity which is shared by patients who are depressed. On the prognostic level, there is a large body of literature that links depressive features in acute schizophrenics to favourable subsequent course (Astrup & Noreik, 1966; Vaillant, 1964). We were, therefore, interested in investigating the relationship of depression with impaired affect and with positive/negative symptoms in young acute schizophrenic patients. We used a systematic multidimensional study of affect impairment among 37 young acute schizophrenic patients in a prospective, longitudinal approach over a 2-year span. In addition to a detailed assessment of the affect profile, including depression, both at baseline and on follow-up, we rated patients clinically for a positive and negative syndrome as well as general psychopathology, and we conducted premorbid and outcome measurements.

Methods

Subjects

The original cohort consisted of 37 newly admitted, young acute in-patients who ranged in age from 18 to 34 years (mean = 24.01). They were chosen from consecutive admissions to an acute care unit of a large state psychiatric facility in the Bronx, New York, which in part serves as an acute receiving hospital. All subjects had a formal DSM–III diagnosis of schizophrenia (American Psychiatric Association, 1980), which was independently confirmed via diagnostic interview by a psychiatrist and a research psychologist, and their length of illness from initial onset was less than 2 years. Cases with questionable diagnosis, known organic disorder, major affective illnesses, and mental retardation were excluded. All patients signed informed consent. The final sample constituted a fairly representative cross-section of acute schizophrenic admissions in the New York City area, including 22 males, 15 females, 22 Blacks, and 15 Whites, who had, on average, a twelfth grade education. Mean duration of illness since first psychiatric hopitalisation was 1.35 years, with 60% of patients having had no or only one previous admission. Further details on sample characteristics are reported elsewhere (Lindenmayer *et al*, 1984, 1986) and described in Table I.

Design

Each patient was assessed 1–2 weeks after index admission on a battery of clinical, psychometric, and historical measures (*infra*). The average follow-up period was 26.5 months after the original assessment (range = 21–33 months). We attempted to recontact all patients first by sending them a form letter and next by personal phone calls asking their participation in an interview.

In addition, we systematically searched the medical records of the hospital where the index admission had occurred as well as those of the area hospitals and their out-patient departments. In this manner, we located 21 former patients, of whom 19 co-operated in reassessment. At this time six subjects (32%) were staying in hospital, while 13 were living in the community. Five of the patients (26%) were drug-free and the remainder were receiving standard neuroleptics, with a dose range from 100 mg to 1200 mg daily in chlorpromazine equivalence (mean = 494 mg) (Ban, 1971).

Although the follow-up represented only 51.4% of the original cohort, our analyses suggested that the follow-up and drop-out samples were comparable on relevant features (see Table I). They proved highly similar in demographic characteristics, such as age, sex, race, marital status, and education. There were also no significant group differences on baseline psychopathological variables, except that drop-outs had a higher mean positive syndrome score. Of particular importance for the present study (infra), the groups were not significantly dissimilar in affective impairment, depression, chronicity of illness, premorbid adjustment to school, negative syndrome, and general psychopathology. We concluded, therefore, that the results derived from the reduced follow-up sample could be cautiously extended to the entire sample.

Baseline measures

After a 30 to 40 minute semi-structured clinical interview, a psychiatrist and psychologist performed independent ratings on the Manifest Affect Rating Scale (MARS). This 16-item scale, modified from the procedure developed by Alpert & Rush (1983), provides a detailed assessment of various affective parameters, such as facial expression, expressive gestures, eye contact, lability, and appropriateness of affect. It is composed of four-point severity ratings, each with descriptive anchoring points along a range from 0 (normal) to 3 (extreme pathology). Previously, we have found the MARS to provide meaningful description of the affective profile of schizophrenics in the acute (Lindenmayer *et al*, 1984) and chronic stages (Opler *et al*, 1984).

Psychopathology was assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay *et al*, 1987, 1988). This 30-item, 7-point severity scale was based originally on the 18-item Brief Psychiatric Rating Scale (Overall & Gorham, 1962) and 12 items from our Psychopathology Rating Schedule (Singh & Kay, 1975). The PANSS adaptation, however,

TABLE I

Comparison of follow-up v. dropout group on demographic, premorbid, and baseline clinical characters

Sample characteristics	*Follow-up groups* (n = *19)*	*Dropouts* (n = *18)*	*Statistical test*
Catergorical variables	*Ratio*	*Ratio*	χ^2 *square*
Sex			
Male:female	11:8	11:7	0.04
Ethnic group			
Black:Hispanic:White	12:5:2	10:5:3	0.36
Marital status			
Single:married	18:1	15:3	1.25
Continuous variables	*Mean (SD)*	*Mean (SD)*	*t*
Age first assessed	23.77 (4.21)	24.33 (4.33)	0.42
Age first hospitalised	22.05 (4.40)	23.33 (4.13)	0.91
Length of illness[1]	20.16 (36.72)	12.00 (18.84)	0.86
Number of previous admissions	1.63 (1.52)	1.00 (1.32)	1.32
Days hospitalised (past 18 months)	79.47 (93.74)	57.53 (24.07)	0.98
Years of education	12.00 (1.32)	12.06 (1.50)	0.13
Premorbid school adjustment	2.42 (1.17)	2.89 (1.08)	1.27
Premorbid work adjustment	1.94 (0.83)	2.33 (1.14)	1.16
General psychopathology	39.04 (12.48)	39.36 (9.28)	0.09
Positive syndrome score	17.26 (5.30)	22.28 (4.76)	3.03[2]
Negative syndrome score	22.05 (7.81)	20.50 (5.09)	0.72
MARS emotional unrelatedness	5.79 (4.25)	4.06 (2.98)	1.44
MARS expressive immobility	2.37 (2.22)	1.28 (1.13)	1.90
MARS inappropriate affect	1.47 (1.22)	1.72 (1.53)	0.55
BPRS depression factor	6.32 (3.23)	5.89 (2.52)	0.45

1. number of months since first psychiatric hospitalisation.
2. $P<0.005$.

introduced strict operational criteria for conducting the clinical interview, for defining all 30 symptoms, and for rating each of seven levels of psychopathology, covering a range between absent and extreme.

For the purpose of identifying a positive and negative syndrome, a positive score was constructed by summing the ratings on delusions, hallucinatory behaviour, conceptual disorganization, excitement, grandiosity, suspiciousness, and hostility. Similarly, a negative score was computed by adding the ratings of another seven psychopathology items: blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking. It should be noted that these items were selected as 'primary negative', or deficit symptoms (cf. Carpenter *et al*, 1985), and did not include parameters likely to derive from positive psychopathology (e.g. poor attention, disorientation), nor parameters most closely identified with depression (e.g. depressed mood, guilt feelings, motor retardation).

Our procedure for syndromal assessment has been used in several studies (Lindenmayer *et al*, 1984, 1986; Kay *et al*, 1986), and has demonstrated sound reliability (alpha = 0.73 and 0.83 for the respective syndromes), stability in chronic unremitted schizophrenics across 6 months (retest r = 0.80 and 0.68 respectively), as well as validity, including construct, concurrent, and predictive type (Kay *et al*, 1987). The remaining 16 items from the PANSS which had not been involved in the positive–negative assessment provide a summated index of general psychopathology. In the present study, the baseline inter-rater reliabilities for the positive, negative ratings and general psychopathology ratings were 0.81, 0.84 and 0.88 respectively. Scores on five distinct clinical dimensions, including anergia, depression, and thought disorganisation, were obtained by combining factor-derived component items according to the BPRS (Guy, 1976).

Disturbance of attention was quantified temporally using the Span of Attention Test (SOA) (Kay and Singh, 1974), a psychometric procedure which gauges the average duration, over two trials, that one concentrates on a routine motor task before showing signs of distractibility. The test also yields a measure of spontaneous psychomotor rate, calculated as the ratio of test items completed to time elapsed. The reliability index of the SOA for schizophrenics, using the test-retest method over a 2-week drug-free period, is 0.82 (Kay, 1982).

Drug induced extrapyramidal symptoms (EPS) were separately evaluated after complete physical examination by use of the 7-item Exprapyramidal Rating Scale (Alpert *et al*, 1978) and the 10-item Abnormal Involuntary Movement Scale (NIMH, 1974).

Subdiagnostic (DSM–III criteria), historical, and demographic data were collected on the basis of patient interviews, staff reports, medical records, and information stored in the hospital's computerised data bank. In addition to the sample characteristics presented in Table I, we secured data on disposition from the index admission (discharged as improved v. a less favourable disposition) and premorbid ratings on school and work functioning. The latter were rendered along a 4-point scale that ranged from 'poor' to 'good' on the basis of reports by the patient, family, therapist, and medical records. Finally, patients' medical records provided data from which we calculated mean daily neuroleptic dose over the past year, as expressed in chlorpromazine equivalence (Ban, 1971).

Follow-up measures

Fourteen outcome measures were obtained at follow-up from clinical, psychometric, and objective indices of functioning. To ensure comparability of ratings, the same research team re-evaluated patients on the MARS, PANSS and SOA to assess later clinical status in terms of affect impairment, general psychopathology, and disturbed attention. These procedures were conducted without reference to prior scores on the measures and without a research hypothesis that might have contributed to an expectancy bias. Other aspects of psychiatric and psychosocial adjustment were measured by consensus ratings on the 5-point Strauss & Carpenter Level of Functions Scale (LFS), a 9-item instrument of demonstrated reliability (Small *et al*, 1984).

Results

Affect components

Factor analysis of the baseline affect ratings in 36 young acute schizophrenics, using principal component method, revealed three distinct affective dimensions: (a) emotional unrelatedness, (b) expressive immobility, and (c) inappropriateness of affect (Table II). The two factors were strongly interrelated ($r = 0.75$, $P<0.001$), and they co-varied also with the PANSS depression factor ($r = 0.69$ and $r = 0.68$, $P<0.001$ respectively), while the third factor was found to be independent on these variables. In addition, Factors 1 and 2 were highly correlated with the negative syndrome ($r = 0.78$ and 0.73, respectively, $P<0.001$), but not the positive ($r = -0.14$ and -0.37, respectively, NS). Factor 3, by contrast, correlated only with a baseline positive syndrome ($r = 0.43$, $P<0.05$). Not surprisingly, the baseline depression factor was also strongly associated with the concurrent negative syndrome ($r = 0.70$, $P<0.001$), pointing to a significant overlap of depression with negative psychopathology as well as emotional unrelatedness and expressive immobility in acute schizophrenics.

Among possible confounding variables, such as age, neuroleptic drug dosage, and EPS, of the four affective dimensions only emotional unrelatedness showed a significant association with EPS ($r = 0.55$, $P<0.02$), suggesting that other affective components were not systematically mediated by control variables and iatrogenic factors.

Reliability

The MARS reliability was examined on 32 patients for whom simultaneous baseline ratings had been performed by two

TABLE II
MARS factor analysis, principal component method

	Factor structure		
MARS items	*Factor 1: Emotional unrelatedness*	*Factor 2: Expressive immobility*	*Factor 3: Inappropriateness of affect*
Facial expression	0.85	0.33	0.19
Expressive gestures	0.88	0.44	−0.02
Vocal emphasis	0.84	0.22	−0.20
Eye contact	0.64	0.40	0.19
Voice level	0.66	0.55	−0.19
Global rating: relatedness	0.94	0.37	0.14
Spontaneous non-communicative movements	0.01	−0.53	0.24
Speech rate	0.52	0.70	−0.31
Response latency	0.49	0.79	0.15
Spontaneity of thought content	0.54	0.78	0.18
Sad affective tone	0.59	0.72	0.14
Affective lability	0.05	−0.20	0.68
Silly affective tone	−0.09	−0.26	0.67
Angry affective tone	−0.17	0.19	0.45
Global rating: inappropriate feelings	0.17	0.25	0.80

TABLE III

Reliability of baseline MARS assessments by three raters

	Inter-rater agreement[1]	*Pearson correlation*[2]	
		r	*P*
Factor 1	0.96	0.90	0.001
Factor 2	0.97	0.87	0.001
Factor 3	0.99	0.86	0.001
Total	0.97	0.84	0.001

1. Concordance within one point.
2. Using the Spearman Brown prophecy formula to anticipate full scale reliability.

psychiatrists and one psychologist. Their degree of agreement across the 16 items ranged from 0.92 to 1.00, with an average of 0.97. As shown in Table III, the inter-rater concordance for the three factors and the corresponding correlations among raters were uniformly high and significant ($P<0.001$). Internal reliability analysis of the MARS, based on split-half comparison of odd-even items and the Spearman-Brown prophecy formula, yielded $r = 0.81$ ($P<0.001$).

Affect and prognosis

The correlations of baseline affect factors with follow-up clinical and functional ratings are presented in Table IV. Of the four affect parameters, only the depression factor showed prognositc value, correlating significantly with several measures of outcome, including overall level of functioning, social relations, and occupational adjustment. Thus a high depression rating at index hospitalisation, but not lesser affect deficit, was predictive of favourable outcome after 2 years.

To examine further the relationship of affect impairment with outcome, we looked at its concurrent association with other variables of known clinical and prognostic import. As Table V shows, the widely reported ominous implications of affect deficit were apparent not at baselines, but only at follow-up, at which time MARS Factors 1 and 2 were significantly correlated with poor level of functioning and unfavourable prior disposition. Whereas depression as observed at the outset forecasted a high functional level 2 years later, this correspondence no longer obtained when the two variables were concurrently assessed in the post-acute phase. MARS Factor 1 was significantly correlated at baseline with depression, but this association was lost at follow-up suggesting that the initial assessment of emotional unrelatedness was partly determined by depressive features. Both Factors 1 and 2 were inversely associated with SOA Attention Span at baseline only; thus, initial observations of emotional unrelatedness and immobility seemed also to be influenced by patients' deficit in attention.

Poor premorbid functioning correlated significantly with emotional unrelatedness only at follow-up. Disposition from past psychiatric hospitalisations, another likely prognosticator, correlated significantly with Factors 1 and 2, also only at follow-up. In terms of schizophrenic subtype, depression ratings were significantly higher among the non-paranoid subjects at baseline, while after 2 years inappropriate affect characterised the paranoids.

Discussion

Our results indicate that affect impairment in young acute schizophrenics can be reliably assessed as a multidimensional construct that differentiates between negative and positive symptoms and carries differing prognostic import. In particular, we identified three

TABLE IV

Prognostic significance of affective impairment: correlations (Pearson r) of baseline affective dimensions with follow-up measures

	Baseline affective dimensions			
	MARS		*PANSS*	
	Factor 1: Emotional unrelatedness	*Factor 2: Expressive immobility*	*Factor 3: Inappropriateness of affect*	*Depression factor*
Follow-up measures				
General psychopathology	−0.08	−0.01	−0.02	−0.31
Positive syndrome	−0.37	−0.26	−0.20	−0.43
Negative syndrome	−0.19	0.02	0.03	−0.31
Follow-up hospitalisation (30 months)	−0.15	0.07	0.13	−0.02
Overall level of function (LFS)	0.33	0.07	0.02	0.52[1]
Quality of social relations (LFS)	0.43	0.12	0.02	0.51[1]
Quantity of useful work (LFS)	0.41	0.33	0.16	0.48[1]
Quality of useful work (LFS)	0.38	0.37	0.02	0.57[2]

MARS = Manifest Affect Rating Scale; PANSS = Positive and Negative Syndrome Scale; LFS = Level of Functions Scale.
1. $P<0.05$.
2. $P<0.005$.

TABLE V

Concurrent correlations of four affect dimensions at baseline assessment (n = *19) and follow-up* (n = *18 for MARS,* n = *19 for PANSS)*

Shown are the results of Pearson *r* analyses and significant differences between correlation coefficients at baseline v. follow-up (t)

	MARS						*PANSS*					
	Factor 1: Emotional unrelatedness			*Factor 2: Expressive immobility*			*Factor 3: Inappropriateness of affect*			*Depression factor*		
	Baseline	*Follow-up*	*t*	*Baseline*	*Follow-up*	*t*	*Baseline*	*Follow-up*	*t*	*Baseline*	*Follow-up*	*t*
General psychopathology	0.73****	0.77****		0.61***	0.81****		0.31	0.68***		0.78****	0.40	
Positive syndrome	−0.14	0.32		−0.37	0.20		0.43*	0.74****	2.14*	−0.24	−0.13	2.10*
Negative syndrome	0.78****	0.83****		0.73****	0.86****		0.23	0.49*		0.70****	0.45*	
Depression factor	0.63****	0.33		0.68****	0.65***		−0.01	−0.06		—	—	
Attention span (SOA)	−0.58**	−0.40		−0.55**	−0.33		−0.05	−0.33		−0.39	0.16	
Psychomotor rate	−0.69****	−0.48*		−0.40	−0.40*		0.03	0.04		−0.50*	−0.08	
Premorbid school	0.12	−0.56**	2.16*	−0.11	−0.30		−0.07	−0.46		0.17	0.03	
Premorbid work	−0.39	−0.38		−0.53**	−0.30		−0.17	−0.19		−0.31	−0.04	
Premorbid mean	−0.09	−0.52*		−0.30	−0.32		−0.12	−0.37		−0.03	0.00	
Favourable disposition	0.00	−0.65***	2.25*	−0.12	−0.54**		−0.16	−0.27		0.04	−0.42	
Nonparanoid subdiagnosis	0.22	−0.28		0.27	−0.34	2.15*	0.01	−0.48*		0.54**	−0.07	2.10*
Follow-up level of function (LFS)	0.33	−0.70****	4.08****	0.07	−0.69****	3.40***	0.02	−0.61***	2.02*	0.52*	−0.20	2.90*

* $P<0.05$; ** $P<0.02$; *** $P<0.01$; **** $P<0.001$.

dimensions of affect impairment which are distinct and clinically meaningful. Emotional unrelatedness and expressive immobility were associated with depression. Inappropriate affect was associated with a positive or florid syndrome and was independent of depression and of a negative syndrome. This could mean that the more the schizophrenic affect is dominated by inappropriateness, the less the affective impairment is associated with depression.

The association of affective withdrawal (MARS Factors 1 and 2) with the depression factor at baseline may be understood as a protective manoeuvre to 'dampen external stimuli in a person whose cognitive and perceptual processes are becoming overwhelmed and dysfunctional' (Carpenter *et al*, 1985). Alternative interpretations of the association of affective withdrawal with depression may be found in Knight & Roff's (1985) observation of 'continued experience of affective deficits, social withdrawal, and isolation leading to increased depression', or in McGlashan & Carpenter's concept of post-psychotic depression (McGlashan & Carpenter, 1976). Both these concepts were derived from observations after the acute phase, and neither one implied favourable outcome as we determined from our acute baseline data. In particular, McGlashan & Carpenter (1979) found that depression at discharge did not predict recovery 1 year later.

The baseline presence of depression in our young schizophrenics raises the question of possible misdiagnosis of patients who qualify as having major affective or schizo-affective disorders. While DSM–III indeed gives little room to the diagnosis of schizo-affective disorder, thereby enhancing the classification of schizophrenia, we systematically deleted from our sample all diagnostically ambiguous cases. Finally, one must consider the possibility that the observed overlap of affective deficits with depression may be an artifact of an unreliable or undiscriminating rating instrument. This difficulty has been a problem for a number of authors (Harrow *et al*, 1977; Andreasen, 1979; Abrams & Taylor, 1978), and its ramifications have been extensively reviewed by Knight & Roff (1985).

They noted that some of the items encompassed by affect rating scales may select for depression rather than for flat affect or may fail to tease apart these different manifestations. We found our rating techniques to be reliable, and several observations suggested independence among some of the affect dimensions assessed: the lack of association between inappropriate affect and the depression factor; the lack of association between emotional unrelatedness and depression in the post-acute phase; the differential correlates with positive and negative syndromes; and, finally, the unique predictive ability of baseline depression, which did not obtain for any of the other affective components.

In terms of prognostic implications, we found, contrary to expectation, that baseline affect deficits did not portend unfavourable outcome in these young acute schizophrenics; only the depression factor was of predictive value, foreshadowing better functioning after 2 years. The latter observation concurs with a body of literature that links depressive features in acute schizophrenics to favourable subsequent course (Vaillant, 1964; Astrup & Noreik, 1966). Gift *et al* (1980) more recently found a 'retardation-bizarreness' cluster associated with good outcome in a group of acute schizophrenics and hypothesised that it could represent a specific depression factor, 'leaving out many symptoms customarily considered pre-eminent in affective disorder'. This observation can be further expanded by our previous follow-up study of positive and negative symptoms, in which we unexpectedly found negative and not positive symptoms to predict good outcome (Lindenmayer *et al*, 1986). The baseline negative syndrome correlated significantly with concurrently assessed depression and was associated with good outcome as well. When depression was statistically removed by partial r, however, 41% of the shared variance between baseline negative score and follow-up level of functioning was retained as exclusive of depression, pointing to a mediating and protective function of deficit symptoms for outcome in these young schizophrenics.

Therefore, while we found that the affective profile consists of several different dimensions that can be reliably assessed, the concurrent and prognostic significance of these dimensions proved to be specific. Clearly, the relationship of depression with affective deficits during the various phases of the schizophrenic disorder is a complex one and needs to be appreciated by the clinician. Further prospective longitudinal studies will be necessary to enhance our understanding of the role of affective deficits and depression in schizophrenia.

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Do Negative Symptoms Respond to Pharmacological Treatment?

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The introduction of neuroleptic (or anti-psychotic) medication into clinical practice was a major advance in the treatment of schizophrenia. Numerous well-controlled, double-blind clinical trials have established the therapeutic efficacy of these agents in both the acute and long-term treatment of schizophrenia (Klein *et al*, 1980; Kane & Lieberman, 1987). In general, the therapeutic benefit of medication has been assessed in terms of the relative reduction in the more florid signs and symptoms of schizophrenia (e.g. hallucinations, delusions, thought disorder, agitation, and hostility) and the ability of maintenance medication to reduce the rate of recurrence of these symptoms and in turn rates of rehospitalisation. At the same time it has been quite apparent that anti-psychotic drugs do not necessarily eliminate some of the major chronic disabilities of patients with this illness, disabilities reflected in impoverished affect, lack of drive and ambition, impaired spontaneity, reduced ability to relate to others, and diminished pleasure capacity. These symptoms have at times been described as negative in that they reflect an absence of or reduction in certain aspects of psychologic, cognitive, and emotional functioning in an attempt to distinguish them from the distortions or exaggerations in normal function which characterise positive symptoms (Strauss & Carpenter, 1974; Jackson, 1904).

In discussing the treatment of negative symptoms with pharmacologic agents it is important to address issues of definition, assessment, and differential diagnosis, as well as the design and methodology of the clinical trial. As has been emphasised by other authors (Pearlson *et al*, 1984; Pogue-Geile & Harrow, 1984) negative symptoms are not unique to schizophrenia and although the clinical presentation may be similar these signs and symptoms may vary in aetiology, course and treatment response between patients and even within patients depending upon the stage of the illness and other factors.

In terms of aetiology, some patients may experience diminished affect, spontaneity and motivation as a result of the extrapyramidal side-effects of neuroleptics, particularly akinesia. These effects can persist into the maintenance phase of treatment, and tolerance does not necessarily occur even after long periods of neuroleptic treatment. Data from dosage reduction studies in the context of long-term treatment (Marder *et al*, 1984; Kane *et al*, 1986) support this conclusion in showing improvement on items such as blunted affect, emotional withdrawal, and psychomotor retardation among those patients receiving low doses of neuroleptics. Therefore, in assessing the impact of pharmacologic treatments on negative symptoms the presence of pseudoparkinsonism should be considered. Strategies such as neuroleptic dosage reduction or a trial of antiparkinsonian medication may be useful in helping to clarify the situation.

Various types of affective disorders should also be considered in the differential diagnosis of negative symptoms. Many patients with schizophrenia experience transient or chronic states of dysphoria. Post-psychotic depression has frequently been described in patients with schizophrenia (Steinberg *et al*, 1967; McGlashan & Carpenter, 1976). The dysphoria which patients experience may range from an 'endogenomorphic' depression with vegetative signs to that associated with severe demoralisation. Although patients with schizophrenia have substantial reason to be demoralised, the assumption is that this state is a more realistic response to a bad situation rather than a depression resulting to a greater degree from non-situational causes. The differentiation of demoralisation from true depression can be difficult, particularly in a situation where the basis for the demoralisation is not likely to recede.

Several studies of antidepressant drugs have been carried out in the treatment of depression occurring in schizophrenic patients (Siris *et al*, 1978, 1987; Prusoff *et al*, 1979). The most rigorous study to date has been conducted by Siris *et al* (1987) and suggests the potential value of imipramine as an effective treatment for patients with depression as defined by specific criteria. In addition, these investigators attempted to rule out akinesia as a contributing factor by treating patients with benztropine mesylate 6 mg/day for one week prior to inclusion in the imipramine trial. Patients randomly assigned to imipramine (plus continued neuroleptic treatment) fared significantly better in terms of their global improvement and in terms of individual symptoms that are components of the depression syndrome. There were no significant differences in psychoses ratings or side-effects between the imipramine and the placebo groups.

Siris *et al* (submitted for publication) also assessed improvement in negative symptoms and reported that of those patients who met their criteria for post-psychotic depression, one-half also satisfied criteria for negative symptoms. The negative symptom patients were rated as more severely ill on global measures, worried more and were more phobic, but did not score higher on ratings of depression. Those negative symptom patients randomly assigned to imipramine did show more improvement than those randomised to placebo on some measures, but not on the specific criterion items for negative symptoms. The items on which imipramine-treated patients did significantly better were psychomotor agitation, self-reproach and negative self-evaluation.

It is also possible that the psychosocial deprivation associated with the illness and/or with chronic institutionalisation can further diminish social drive, affect, pleasure capacity, etc, however, it is difficult to distinguish cause and effect in this context. At the same time, in some patients withdrawal and apparent apathy may serve an 'adaptive' function for an individual who is attempting to reduce uncomfortable or disorganising stimuli, experience or affective states.

Pharmacological treatment of negative symptoms

Evaluating the effects of anti-psychotic drugs on negative signs and symptoms is complicated by the fact that some dimensions of the negative symptom spectrum may respond if they occur in the context of an acute exacerbation of positive symptoms as well. The extent to which negative symptoms in this context are secondary to the positive symptoms or are different manifestation of the same underlying pathophysiology is not clear, but the evidence from clinical trials is that negative symptoms do improve along with positive symptoms (Goldberg *et al*, 1965, 1985). After the resolution of an acute exacerbation, however, many patients are left with residual negative symptoms which are more persistent and less responsive to neuroleptics. Carpenter *et al* (1985) have argued that it is these symptoms or deficits which should be considered as core features of the schizophrenic illness and be conceptualised as primary negative symptoms. The extent to which these phenomena may be manifestations of a specific subtype of the schizophrenic illness is obviously an area of enormous potential clinical and heuristic significance.

In any attempt to review the pharmacologic treatment of negative symptoms it is important to keep in mind that the differential diagnostic considerations which we have described have not been fully attended to.

Are specific neuroleptics more effective in alleviating negative symptoms?

By and large most clinical trials of different neuroleptics or neuroleptic classes have not shown significant superiority of one drug or drug class over another in the treatment of negative (or positive) symptoms.

There has been some suggestion that the diphenylbutylpiperidines (pimozide, clorpimozide, fluspirilene and penfluridol) might be superior in the treatment of negative symptoms.

Kolivakis *et al* (1974) studied 51 patients who were randomly assigned to pimozide or chlorpromazine in a double-blind 24-week trial. Patients had been stabilised on other drugs for 2 weeks prior to the trial. The average dose of pimozide was 7 mg/day and for chlorpromazine 216 mg/day. Patients improved on both drugs, but pimozide was more effective in alleviating emotional withdrawal.

Chouinard & Annable (1979) compared pimozide and chlorpromazine in 40 newly admitted schizophrenic patients in a 4-week double-blind trial. Chlorpromazine was found to be superior on the tension item, but no other statistically significant differences were observed.

Frangos *et al* (1978) compared fluphenazine decanoate and fluspirilene in 50 chronic patients who had spent at least 2 years in a hospital. The trial lasted 16 weeks with a mean dose of fluspirilene of 12 mg im each week and fluphenazine decanoate 76 mg im every 2 weeks. Fluspirilene appeared to have some superiority on the NOSIE-30, suggesting advantages in areas of socialisation.

Haas & Beckman (1982) compared pimozide dosages of 40–60 mg/day for 4 weeks in 30 schizophrenic in-patients. Although there were no significant differences between groups on the Clinical Global Impressions (CGI) or Brief Psychiatric Rating Scale (BPRS) total score, the pimozide-treated patients did have greater improvement on blunted affect and the anergia factor.

Lapierre & Lavallee (1975) compared penfluridol 20–120 mg/week and fluphenazine 3–18 mg/day in 41 out-patients in a trial which lasted 1 year. There was a trend for patients to exhibit more improvement on emotional withdrawal during penfluridol treatment.

Lapierre (1978) also compared pimozide (mean dosage 6 mg/day) and fluphenazine (mean dosage 7.5 mg/day) in 32 schizophrenic out-patients for 16 weeks. There were no significant differences on BPRS scores, but pimozide patients showed more affective involvement and appropriateness in interpersonal relationships observed during group therapy sessions.

Although in general these investigations do suggest some superiority for the diphenylbutylpiperidines, the overall impression is not one of substantial differences as compared to other drugs. When there are differences, they do tend to favour this class of drugs, but a major concern in these and other studies is the issue of dose equivalency and whether one group is experiencing more extrapyramidal side-effects than another. Even when attempts are made to rate parkinsonian side-effects, subtle differences between groups may not be apparent, though they may influence the behavioural ratings.

Clozapine is an atypical anti-psychotic drug which belongs to the chemical class of dibenzodiazepines, related chemically to the anti-psychotic drug loxapine, however, its pharmacologic characteristics are different from those of loxapine. Unlike typical neuroleptic drugs, clozapine produces only slight, transient eleviations in serum prolactin levels in patients, even on moderate to high doses. Although this drug has generated considerable interest on both clinical and pre-clinical grounds, its development has been delayed because of an increased risk of agranulocytosis.

A recently completed double-blind comparison of clozapine and chlorpromazine in carefully selected, treatment refractory patients is relevant to the present discussion because clozapine proved to be significantly superior to chlorpromazine in both positive and negative symptoms (Kane *et al* 1988). Patients participating in the trial met DSM–III criteria for schizophrenia and were considered treatment resistant based on the following criteria: (a) at least three periods of treatment in the proceeding 5 years with neuroleptic agents (from at least two different chemical classes) at doses equivalent to 1000 mg/day of chlorpromazine or higher for a period of 6 weeks, each without significant symptomatic relief, and (b) no period of good functioning within the proceeding 5 years. In addition, patients had to meet the following psychopathologic severity criteria: total Brief Psychiatric Rating Scale (BPRS) score of at least 45 plus a minimum CGI rating of 4 (moderately ill). Item scores of at least 4 (moderate) were also required on two of the following four BPRS items: conceptual disorganisation, suspiciousness, hallucinatory behaviour, and unusual thought content.

Those patients who met both the historical and severity criteria underwent a prospective period of treatment with haloperidol, 60 mg/day or higher. Those patients who failed to improve as defined by *a priori* criteria were then randomly assigned to clozapine up to 900 mg/day or chlorpromazine plus benztropine, up to 1800 mg/day and 6 mg/day respectively. The double-blind trial lasted for 6 weeks. Significantly greater improvement was seen on all of the positive symptom psychotic measures on the BPRS and in addition clozapine was superior to chlorpromazine on the items of emotional withdrawal, blunted affect, psychomotor retardation and disorientation. The use of prophylactic benztropine mesylate in all patients receiving chlorpromazine minimises the possibility that these differences were due to parkinsonian side-effects occurring in the context of chlorpromazine treatment whereas clozapine has a low propensity to produce such adverse effects. These results are certainly encouraging in suggesting that even among treatment refractory patients who have been symptomatic for long periods of time that some improvement can be brought about with appropriate pharmacologic agents. These data do fall into the pattern previously discussed where negative symptoms respond in conjunction with positive symptoms, however, the treatment-resistant nature of this patient sample makes these results somewhat unique. Clearly a subsequent trial focusing on patients selected specifically for negative or deficit symptoms in the absence of significant positive symptoms would be of particular interest with clozapine.

Other pharmacological agents

A variety of other pharmacologic agents have been utilised in the treatment of negative symptoms. Drugs which enhance dopaminergic transmission, e.g. L-dopa and amphetamine, have been reported to be useful in some patients when combined with neuroleptic drugs (Inanaga *et al*, 1972; Gerlach & Luhdrof, 1975; Cesarec & Nyman, 1985). However, an exacerbation of positive symptoms may occur with these agents in some patients, though this appears to be infrequent. In evaluating the potential efficacy of these compounds, particularly L-dopa, it is important to rule out the presence of extra-pyramidal side-effects to the extent possible to assure that an improvement in negative symptoms is not merely a reduction in pseudoparkinsonism.

Propranolol (Sheppard, 1979; Eccleston *et al*, 1985) and alprazolam (Wolkowitz *et al*, 1986) have also been reported to be helpful in some patients with negative symptoms, but positive studies are limited and require replication.

Bucci *et al* (1987) reported on 30 out-patients with predominant negative symptoms, treated with tranylcypromine plus a neuroleptic, and found improvement in the majority of patients as well as reduced need for anti-parkinsonian medication, but the extent to which this relates to the previous discussion of post-psychotic depression is not clear.

In conclusion, the treatment of negative symptoms remains a challenge. The results of clinical trials to date are suggestive that negative symptoms may be responsive to various pharmacologic agents, however, issues of differential diagnosis remain critical in the clinical assessment and potential treatment of negative symptoms. In addition, we have few data on the extent to which gains brought about by specific pharmacologic treatments are sustained for long periods of time and what impact they have on the long-term course of the illness.

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Three Syndromes in Chronic Schizophrenia

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In recent years, exploration of the distinction between positive and negative symptoms of schizophrenia has provided a fruitful basis for attempts to relate the clinical features of schizophrenia to the accumulating evidence of brain abnormalities in schizophrenic patients. By 1982, there was an extensive body of evidence supporting the hypothesis that negative schizophrenic symptoms, such as poverty of speech and flatness of affect, were associated with substantial brain abnormalities, such as increased ventricular to brain ratio, and extensive cognitive impairment (Crow, 1980; Andreasen & Olsen, 1982). However, at that stage there were several fundamental unanswered questions about the nature of negative symptoms, and their relationship to indices of brain abnormality. This paper presents some findings of a series of studies initiated in 1982 to seek answers to some of these questions.

Negative schizophrenic symptoms tend to be persistent, and positive symptoms tend to be transient, but this is not always the case. Negative symptoms can be transient, while positive symptoms can persist. The partial overlap between the positive–negative dichotomy and the distinction between acute and chronic symptoms, gives rise to the question: is the observed association between negative symptoms and indices of substantial brain abnormality a reflection of a primary relationship between *persistence of symptoms* and brain abnormality, or is the observed association primarily determined by the *type of symptom*. The first issue to resolve in an attempt to answer this question is whether or not persistent schizophrenic symptoms segregate into positive and negative syndromes.

The segregation of chronic schizophrenic symptoms

In the first study of this series, Liddle (1987*a*) studied the correlations between symptoms in a group of 40 schizophrenic patients with persistent symptoms, during a stable phase of their illness. In order to discriminate against the selection of patients suffering from an acute exacerbation of symptoms, all patients who had had an increase in medication or readmission to hospital in the preceding 6 months were excluded.

In this group of patients with persistent symptoms, the segregation of symptoms was only partially congruent with the prediction of a positive–negative dichotomy. The symptoms segregated into three syndromes: Psychomotor poverty (poverty of speech; flatness of affect and decreased spontaneous movement); Disorganisation (disorders of the form of thought; inappropriate affect); and Reality distortion (various delusions and hallucinations). The mutual correlations between symptoms within each syndrome were high, but the correlations between symptoms from different syndromes were low. The syndromes were not mutually exclusive. Some patients suffered from more than one syndrome. Therefore, the syndromes do not constitute separate illnesses. Rather, the findings suggest that there are several distinguishable but overlapping pathological processes in chronic schizophrenia.

Association between syndromes and neuropsychological impairment

A comprehensive battery of neuropsychological tests was administered to the patients participating in the first study, and the relationship between performance in these tests and syndrome scores was examined (Liddle, 1987*b*). Each of the three syndromes exhibited a specific pattern of association with neuropsychological impairment. Psychomotor poverty was associated with impairment of abstract reasoning and long-term memory; Disorganisation was associated with poor concentration and impaired ability for new learning; while Reality distortion exhibited very limited association with neuropsychological impairment, being only weakly correlated with poor performance in figure-ground perception. Both the Psychomotor poverty syndrome and the Disorganisation syndrome, but not the Reality distortion syndrome, were associated with neurological signs indicating impaired cortical processing of sensory information and poor motor coordination.

Proposed localisation of underlying brain abnormalities

The association of each syndrome with a characteristic pattern of neuropsychological impairment suggests that the three syndromes are associated with three different patterns of brain malfunction. Comparison of the clinical features of each syndrome with the sequelae of focal brain injury suggests that the three syndromes might arise from abnormality of three different brain regions (Liddle, 1987*b*). As indicated in Table I, the Psychomotor poverty syndrome and the Disorganisation

TABLE I

Syndromes resulting from brain injury which resemble syndromes of chronic schizophrenia

Syndrome due to brain injury	*Chronic schizophrenic syndrome*
Pseudodepression (Dorsal prefrontal)	Psychomotor poverty
decreased conversation	poverty of speech
flat affect	flat affect
slowness	decreased spontaneous movement
apathy	
Pseudopsychopathy (Orbital prefrontal)	Disorganisation
shallow, silly affect	inappropriate affect
inability to maintain specific meanings	disorders of the form of thought
garrulous speech	poverty of content of speech
Psychosis of temporal lobe epilepsy (Medial temporal lobe)	Reality distortion
hallucinations	hallucinations
delusions	delusions

syndrome resemble two distinguishable syndromes produced by frontal lobe injury (Blumer & Benson, 1975), suggesting that these two chronic schizophrenic syndromes might be associated with malfunction of different regions of the prefrontal cortex. The Reality distortion syndrome resembles the inter-ictal psychosis of temporal lobe epilepsy, which is characterised by delusions and hallucinations, but relatively little flattening of affect or disorder of the form of thought (Parnas & Korsgaard, 1982).

Replication of the segregation of symptoms

The next study in the series was an attempt to confirm the segregation of chronic schizophrenic syndromes into three syndromes, in a separate group of patients. For this study, all of the patients satisfying DSM–III criteria for schizophrenia resident in two long-stay wards and a rehabilitation ward at Horton Hospital, Epsom, were assessed. In general, the patients in this study were more severely impaired than the patients in the first study, and the mean duration of illness for this group was much greater. Symptoms were assessed by a clinician (TREB) who was blind to the details of the segregation of symptoms found in the previous study. Examination of the correlations between symptoms in this second group of patients revealed that the symptoms segregated into three syndromes which were virtually identical to the three syndromes identified previously (Liddle & Barnes, in preparation).

The relationship between syndromes and indices of frontal lobe malfunction

In view of the circumstantial evidence suggesting that the Psychomotor poverty syndrome and the Disorganisation syndrome are associated with malfunction of the prefrontal cortex, a battery of neuropsychological tests designed to assess frontal lobe function, was administered (by DM) to a group of chronic schizophrenic inpatients, aged less than 65, at Horton Hospital. Symptoms were assessed by a clinician (PFL) who was blind to the patients' performance in the neuropsychological tests (Liddle *et al*, in preparation).

Examination of the correlations between test performance and syndrome scores revealed that both the Psychomotor poverty syndrome and the Disorganisation syndrome were associated with impairment in frontal lobe tests. Psychomotor poverty was associated with decreased verbal fluency, and impaired performance in the Stroop test, while the Disorganisation syndrome was associated with decreased verbal fluency, increased number of perseverative errors in the Wisconsin Card Sorting test and poor performance in the Reitan Trails B test. There were no significant correlations between Reality disortion syndrome score and performance in the frontal lobe tests.

It is necessary to be cautious in interpreting these results because the localising value of neuropsychological tests is limited by the complexity of interrelations between different parts of the brain. Nonetheless, the findings are consistent with the proposal that the Pschomotor poverty syndrome and the Disorganisation syndrome are associated with malfunction of different neuronal systems involving the frontal lobes.

The relationship between syndromes and cortical neurological signs

In the group of patients studied initially, Liddle (1987*b*) had found a correlation between cortical neurological signs and both the Psychomotor poverty syndrome, and the Disorganisation syndrome. The group of patients who completed the tests of frontal lobe function described above were examined for abnormalities of processing of sensory information and motor co-ordination, by a clinician (SH) who was blind to the assessment of the patients' symptoms. The examination tested for sensory signs such as astereognosis, dysgraphaesthesia, and sensory inattention, and for motor signs such as poor co-ordination of finger–thumb opposition, and impaired sequencing in tasks such as the sequential presentation of fist, edge of hand and palm. Examination of the correlation between neurological signs and syndrome scores revealed that both the Psychomotor poverty syndrome score and, to a lesser extent, the Disorganisation syndrome score were significantly associated with abnormal neurological signs (Liddle *et al*, in preparation).

In the case of the Psychomotor poverty syndrome, the correlations with impaired motor co-ordination tended to be higher than the correlations with impaired processing of sensory information, but the differences between the correlations with motor and sensory abnormalities were not statistically significant. Both motor and sensory neurological sign scores were significantly correlated with impaired performance in frontal lobe tests. The correlations of impaired frontal lobe test performance with motor neurological signs tended to be higher than the corresponding correlations with sensory signs.

Hypothesis

There is extensive evidence (reviewed by Liddle, 1988) from studies of phylogenetic development, neuronal connections, and function of the prefrontal cortex in mammals, indicating that there are two distinguishable, but overlapping prefrontal–subcortical–hippocampal neuronal systems. One system involves dorsal structures and the other ventral structures. The dorsal system, which comprises the dorsal prefrontal cortex, anterolateral part of the head of the caudate, cingulate gyrus and hippocampus, plays a major role in the temporal structuring of behaviour in monkeys, and appears to be important for the initiation of activity in man. The ventral system, which comprises orbital prefrontal cortex, ventral part of the head of the caudate (nucleus accumbens), insula, cortex of the temporal pole, amygdala and hippocampus, is concerned with the inhibition of interference from irrelevant influences.

Furthermore, there is evidence from the study of rats, that the prefrontal cortex plays a role in regulating subcortical dopaminergic activity, possibly via corticofugal glutaminergic neurons (Scatton *et al*, 1982). The prefrontal cortex plays an important role in the response to stress. In rats subjected to isolation, prefrontal dopamine activity decreases while there is a reciprocal increase in subcortical dopamine activity, and the animals become more sensitive to stress (Blanc *et al*, 1980). An animal with a prefrontal lesion might be expected to be especially sensitive to stress, and to be prone to subcortical dopaminergic hyperactivity during stress, due to lack of the cortical regulation of subcortical dopamine activity.

There are also substantial glutaminergic projections from the archicortex of the medial tempral lobe, especially from the hippocampus, to the caudate nucleus, and there is evidence that these projections modulate subcortical dopaminergic activity (Hamilton *et al*, 1986).

In the light of these observations from studies of animals, the evidence we have presented concerning the three syndromes of chronic schizophrenia suggests that schizophrenic patients might suffer from persistent malfunction of prefrontal cortex and/or medial temporal cortex. Those with severe malfunction of the prefrontal cortex would exhibit persistent impoverishment or disorganisaton of behaviour. The relative severity of the Psychomotor poverty syndrome and the Disorganisation syndrome would be expected to depend on the relative degree of malfunction of the dorsal and orbital prefrontal cortex. At times of stress, patients with malfunction of the prefrontal cortex would be at risk of developing psychotic symptoms because of impaired regulation of subcortical dopaminergic neurons. Those patients in whom the major malfunction is in the medial temporal lobe, would tend to suffer persistent delusions and hallucinations (Reality distortion syndrome) as a result of persistent impairment of regulation of subcortical dopamine activity by glutaminergic neurons from the hippocampus.

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The Prognostic Significance of Negative Symptoms in Schizophrenia

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As is evidenced by this special supplement of the *British Journal of Psychiatry*, negative symptoms have become the focus of an increasing research effort. We have recently reviewed this overall body of research in an attempt to understand its current status and to suggest directions for future work from a broad perspective (Pogue-Geile & Zubin, 1988). In contrast, the aim of this paper is to review concisely one specific aspect of this research — namely the prognostic and longitudinal characteristics of negative symptoms. Research findings on this general topic will be reviewed by addressing a series of more specific subquestions, which are outlined below. Throughout, the potential importance of *when* in the course of the disorder (i.e. during an acute episode or afterward) negative symptoms are assessed will be emphasised (Kay *et al*, 1986*b*).

Are negative symptoms prognostic of later poor functioning?

Although blunted affect (generally considered one of the primary negative symptoms) was among the earliest characteristics thought to be prognostic of later poor role functioning in schizophrenia when it was present during an acute episode (Langfeldt, 1937), few of the early studies of this hypothesis were methodologically satisfactory. Nevertheless, among the strongest of these earlier studies, several did find blunted affect, when assessed during the acute inpatient episode, to be prognostic of later poor functioning among schizophrenic patients (Astrup *et al*, 1962; Astrup & Noreik, 1966; Carpenter *et al*, 1978; Holmboe *et al*, 1968; Stephens, 1970; Carpenter *et al*, 1978; Knight *et al*, 1979; WHO, 1979; Ciompi, 1980; Knight & Roff, 1985), although several did not (Bland *et al*, 1978; Gift *et al*, 1980). Two more recent studies of the prognostic importance of current negative symptom scales also did not find them to be predictive of later poor functioning when assessed during an acute inpatient episode (Johnson *et al*, 1979; Lindenmayer *et al*, 1986, see also Lindenmayer & Kay, this volume).

The studies of the prognostic importance of negative symptoms assessed during the acute episode are thus mixed in their findings. These inconsistencies among studies may be due to a range of factors, with variations in the breadth of the definition of schizophrenia, measurement of negative symptoms, and chronicity of the samples probably being most important. Therefore, although there is some evidence overall that negative symptoms assessed during acute episodes may be prognostic of later poor functioning among patients diagnosed according to modern narrow criteria, this issue is by no means closed and further, more methodologically adequate, studies are needed to resolve it.

In contrast to these mixed findings regarding the prognostic importance of negative symptoms when they are assessed during an acute inpatient episode, both studies to date of negative symptoms assessed during the post-hospital period have found them to be prognostic of later poor functioning (Pogue-Geile & Harrow, 1985; Biehl *et al*, 1986; Schubart *et al*, 1987). Pogue-Geile & Harrow (1985) reported that negative symptoms initially assessed 2 years after discharge significantly predicted poor overall functioning 2 years later among narrowly diagnosed schizophrenic subjects. This association also held among only first-admission patients. In addition, this study found that the prognostic importance of negative symptoms was due to their occurrence in a subgroup of patients who were already functioning poorly at the initial follow-up and who tended to continue to function poorly at the second follow-up. The second study on this issue was sponsored by the World Health Organization (WHO) (Biehl *et al*, 1986; Schubart *et al*, 1987; see also Biehl *et al*, this volume) and employed an epidemiologically representative sample of first-admission schizophrenic patients who were systematically followed for a total of 5 years. In this unique sample, negative symptoms assessed 6 months after admission significantly predicted overall functional disability at 1, 2, 3 and 5 years after admission.

To summarise, the data are mixed regarding the prognostic importance of negative symptoms assessed during the height of an acute episode, whereas the evidence appears somewhat clearer on the prognostic value of negative symptoms that have been assessed after an acute episode. This may be because negative symptoms that have presumably persisted since the acute episode are more likely to continue to persist, and because negative symptoms assessed during the post-acute period may be less likely to reflect 'secondary' deficits such as medication side-effects and adaptive responses to florid psychosis (Carpenter *et al*, 1985).

Are negative symptoms associated with poor functioning prior to in-patient admission

A large literature exists which suggest some prognostic importance for social and instrumental functioning prior to in-patient hospital admission (i.e. 'premorbid' functioning) in predicting functioning later in the course of schizophrenia (Stoffelmayr *et al*, 1983). Therefore, to the extent that negative symptoms also predict later poor social and instrumental functioning, their association with poor functioning prior to hospital admission is important.

Educational level is one of the most objective and most studied indexes of instrumental functioning prior to hospital admission. To date, five studies have found low educational achievement to be significantly predictive of increased negative symptoms assessed during in-patient periods in hospital (Johnstone *et al*, 1981; Andreasen & Olsen, 1982; Oper *et al*, 1984; Kay *et al*, 1986*a*) or after hospital admission (Pogue-Geile & Harrow, 1984), but five studies have not (Green & Walker, 1985; Kay *et al*, 1986*b*; Liddle, 1987; Owens & Johnstone, 1980; Pogue-Geile & Harrow, 1987). In contrast to these mixed findings regarding educational achievement, all three studies that have investigated asociality prior to hospital admission have found it to significantly predict later negative symptoms (Andreasen & Olsen, 1982; Pogue-Geile & Harrow, 1984; Breier *et al*, 1987). Although most of these studies were not restricted to first-admission cohorts, Pogue-Geile & Harrow (1984) found both low education and asociality to predict later negative symptoms among a subsample of first-admission patients. In addition, this study assessed negative symptoms at follow-up after discharge, and functioning at in-patient admission, thus reducing any potential recall bias based on the patient's current state. One study has also suggested that this association between poor functioning before hospital admission and later negative symptoms is significant only among schizophrenic and not among non-schizophrenic patients (Pogue-Geile & Harrow, 1986).

It is difficult to tell from these data whether poor early functioning may be a risk factor for the development of negative symptoms, or whether these early functioning deficits may reflect nascent negative symptoms. In either case, they suggest a probable association between negative symptoms and earlier social and instrumental functioning deficits that is consistent with some prognostic importance for negative symptoms.

Are negative symptoms concurrently associated with poor social and instrumental functioning?

In order to better understand any prognostic importance of negative symptoms for later functioning deficits, it is important to determine their concurrent association with such deficits.

All four studies of this question have found a significant association between negative symptoms, assessed following hospital discharge, and current social and instrumental functioning deficits among schizophrenic patients (Johnstone *et al*, 1979; Pogue-Geile & Harrow, 1984; Biehl *et al*, 1986; Lindenmayer *et al*, 1986). However, as was pointed out by Pogue-Geile & Harrow (1984), although poor functioning generally was present among patients with negative symptoms (75%), poor functioning also occurred frequently among patients who did not show marked negative symptoms on interview (41%). Such results make it clear that although negative symptoms tend to be associated with deficits in role functioning, there are clearly other 'pathways' to poor psychosocial functioning.

Are negative symptoms stable over time?

The one study that has investigated the short-term stability of the negative symptom, poverty of speech, during the first few weeks of an acute episode (Harvey *et al*, 1984) found significant test–retest correlations and an apparently non-significant trend toward decreasing mean levels of poverty of speech. In a related study of acute episodes, significant test–retest stability was also found for poverty of speech across two consecutive hospital admissions (Earle-Boyer *et al*, 1986), which would suggest a stability in negative symptoms between different acute episodes.

The degree of stability of negative symptoms between an acute episode and the early post-episode period is important for understanding any potential prognostic importance of negative symptoms that are present during an acute episode. However, both of the two studies of this question found non-significant test–retest correlations for negative symptoms between in-patient and early post-discharge assessments (Lindenmayer *et al*, 1986; Ragin *et al*, 1989). Other studies have reported only on changes in mean level of negative symptoms between inpatient and early (within 1 year) post-discharge periods, with two studies reporting no significant mean change (Andreasen *et al*, 1985; Lindenmayer *et al*, 1986), one a significant increase (Ragin *et al*, in press) and two reporting significant mean decreases in negative symptoms between inpatient and post-discharge assessment (WHO, 1979; Biehl *et al*, 1986). The latter reports from the Mannheim WHO project and the International Pilot Study of Schizophrenia had the largest samples of these studies and thus should carry more weight, suggesting that negative symptoms probably decrease following an acute episode.

In contrast, the stability of individual differences among patients with negative symptoms may be greater during the post-hospital period (i.e. 2–5 years after discharge). To date both studies of this issue have found significant test–retest correlations for negative symptoms when repeatedly assessed during the early post-hospital period (Biehl *et al*, 1986; Pogue-Geile & Harrow, 1985). However, these studies differ somewhat in their findings regarding changes in the average level of negative symptoms during the 5 years following hospital discharge, with Pogue-Geile & Harrow (1985) observing that negative symptoms tended to decrease, although not significantly so, between assessments 2 to 5 years after discharge, whereas the Mannheim WHO study found a steady and probably significant increase in negative symptoms during this period (Biehl *et al*, 1986).

Although perhaps the later course of negative symptoms is even more important theoretically than their early course, only two studies have investigated this. Pfohl & Winokur (1982, 1983) found, based on chart notes, consistently high levels of negative symptoms during the second decade after first hospital admission, and among patients in their 50s, Johnstone *et al* (1986) reported significant test–retest correlations over a 4-year period with poverty of speech significantly increasing, and flat affect significantly deceasing during this time. However, both of these studies used in their samples patients who had been continuously admitted for periods in hospital between assessments, and therefore their findings are potentially biased toward finding symptom stability, since any patients whose symptoms remit may be discharged and thus not be included in the sample.

One final point concerns the comparison between the stability of negative symptoms among schizophrenic and non-schizophrenic patients (Pogue-Geile, in press). Although several studies have found that levels of 'negative symptoms' are equivalent between schizophrenic and depressed patients during the in-patient period (Andreasen, 1979), one cross-sectional study (Pogue-Geile & Harrow, 1984) and one longitudinal study (Ragin *et al*, 1989) have found that schizophrenic patients show higher levels of negative symptoms than depressed patients after discharge from hospital. These studies suggest that negative symptoms are more persistent following an acute episode in schizophrenia than in depression.

In summary, these studies suggest more changes in negative symptoms than might have been originally expected given hypotheses about their putative relationship with structural brain abnormalities. This appears to be particularly true regarding the transition between acute episodes and post-episode periods. In contrast, negative symptoms appear to be more stable during the post-episode periods, although even here changes are not uncommon.

Summary and Implications

Negative symptoms appear to be moderately associated with deficits in social and instrumental functioning among schizophrenic patients. This association appears to be not only concurrent, but also to extend through time, both before and after hospital admission. The available data thus suggest some modest prognostic utility for negative symptoms in predicting later impaired life functioning, which may be somewhat less for negative symptoms that are assessed during the height of an acute episode compared with those assessed after the acute period. In any case, the prognostic utility of negative symptoms is modest, with many schizophrenic patients functioning poorly without negative symptoms. It is thus clear that negative symptoms are not the only 'pathway' to poor social and instrumental functioning. What prognostic utility that is present appears to result from the tendency of negative symptoms to occur in a subgroup of patients who are already functioning poorly and who will tend to continue to show impaired role functioning later during the course of their disorder.

Negative symptoms show some stability during the early course of schizophrenia, although perhaps not as much as has been hypothesised. Substantial change may occur, particularly following an acute episode. As has also been suggested by Kay *et al* (1986*a*), there appears to be some difference between negative symptoms that are present during an acute episode and those that occur after it, with the former appearing to have less prognostic importance and less stability. It also appears that the level of negative symptoms tends to decrease soon after an acute episode. However, it is largely unknown whether the stability or frequency of negative symptoms increases during the later course of schizophrenia (e.g. 10 years after onset).

Although representing our best estimates at this time, these conclusions must nevertheless be regarded as tentative due to several pervasive methodological problems and a shortage of relevant studies. Specifically, few of the studies cited here used samples of first-admission patients or presented such data separately. As has been pointed out by Strauss & Carpenter (1974), established chronicity in samples with varying duration of disorder may lead to spuriously inflated findings of prognostic utility and stability. Future longitudinal studies should employ first-admission patients or report their data separately. Secondly, there was substantial variation among the studies in their measurement and definition of negative symptoms. The degree of similarity among these different definitions is unclear and combining studies which use different definitions may be inappropriate. Future studies should combine a standard narrow definition of negative symptoms (e.g. flat affect and poverty of speech) for comparison purposes with other more experimental rating scales in a 'polydiagnostic' approach. Thirdly, none of the studies cited above controlled medication, and most did not report medication analyses. This is an obvious and potentially important variable whose effects on the prognostic utility and stability of negative symptoms are largely unknown.

In terms of specific topics requiring further research, longitudinal studies of the transition between acute episodes and the post-acute period among first-admission patients are crucial. The stability and prognostic value of negative symptoms during an acute episode are important clinical issues that currently rest on too few findings. More difficult, but also important are studies later in the course of the disorder. Many hypotheses exist concerning a putative increase in stability and frequency of negative symptoms over time, but there are almost no data on these points.

One overall point to be drawn from this review is that negative symptoms appear to be moderately associated, both cross-sectionally and longitudinally, with impairments of social and instrumental role functioning. How might this come about? It appears unlikely that life failures are sufficient to lead to negative symptoms for most patients because many schizophrenic patients experience poor social and occupational functioning, but do not show marked negative symptoms (Pogue-Geile & Harrow, 1984). Rather, it seems more plausible that negative symptoms themselves interfere with adequate role functioning, or alternatively that some common factor disrupts both processes associated with emotional expressivity and also other abilities required for social and instrumental functioning. To date, little work has been done to specify how negative symptoms might interfere with role functioning. An important first step might be to examine patients' own explanations of the effects of negative symptoms on their life functioning. Strauss *et al* (1981, 1985) have championed this approach in attempting to understand the origins of instrumental impairment among patients.

A second major point of this review is that negative symptoms, although moderately stable (particularly during the post-acute period), appear less stable than has generally been hypothesised. In addition to attesting to measurement unreliability, the degree of instability shown argues against a simple model in which all negative symptoms are due to a persisting structural brain abnormality (Crow, 1980, 1985). Rather, these data are consistent with a heterogeneity of negative symptoms as has been proposed by Carpenter *et al* (1985), in which some negative symptoms reflect transient effects of over-medication, for example, and others reflect a more enduring process. Based on this model, a major question is whether these hypothesised aetiologically different kinds of negative symptoms can be distinguished observationally. Alternatively, it may be that negative symptoms still reflect a homogeneous and necessary diathesis, but that their manifestation is to some extent environmentally modulated. Rather than stressing the differences among negative symptoms, this model emphasises their similarity and the importance of determining their underlying diathesis. In addition, this model attempts to account for individual differences in response to putative negative symptom-inducing experiences, since it is unlikely that all patients respond equally to over-medication or social isolation. It is time for some of these more complex hypotheses of negative symptoms to be evaluated (Pogue-Geile & Kashavan, in press).

To conclude, this paper has attempted to summarise both our current knowledge and ignorance of the longitudinal aspects of negative symptoms. Research on negative symptoms to date has made substantive gains, but further work is needed to confirm some of our basic observations, and to expand our theoretical perspectives.

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Psychological and Social Aspects of Negative Symptoms

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Our reintroduction of the concept of negative symptoms in schizophrenia (Strauss *et al*, 1974) has been followed by much productive research on this topic. As in the work of Andreason, Crowe, and others, the focus of most of this research has been on improving descriptive assessments of these symptoms (Andreason, 1982) and exploring their biological correlates (Crowe, 1981). This work has been extremely important, but psychological and social aspects of negative symptoms are also important (Barton, 1959; Wing & Brown, 1970; Gruenberg, 1967), and in these areas there has been little research. Nevertheless, it is crucial to explore possible psychological and social factors in negative symptoms in order to understand the symptoms more fully and to provide a basis for more adequate prevention and treatment. It is also important to clarify psychological and social factors in these symptoms to provide a basis for more effective biological research, since the heterogeneity of negative symptoms at a psychological level could hide significant biological correlates.

In this paper we will explore the possible psychological and social aspects of negative symptoms utilising information from our intensive longitudinal studies and from large sample studies, first-person accounts, and clinical experiences. Based on these sources, we will develop two hypotheses: (a) Negative symptoms arise in many instances as responses to extremely difficult psychological and social situations. These symptoms may even serve to help the person with schizophrenia survive. In such instances, the term 'negative symptoms', although descriptively useful, may be misleading, since these symptoms may reflect active coping on the part of the patient; (b) Negative symptoms have a psychological and social impact on the further course of disorder. Negative symptoms may provide some psychological solutions for the problems patients encounter, but these symptoms may also generate a cyclical feedback process that removes patients from social functioning and in this way reduces the likelihood of improvement. This impact may contribute to the poor prognostic implications of negative symptoms.

Thus, in this paper we develop further our thesis that as part of understanding severe mental disorders and improving their treatment, one must use an interactive developmental model (Strauss & Carpenter, 1981). This approach requires viewing persons who have these disorders as complex evolving systems operating in biological and social contexts. Negative symptoms arising from psychological, biological, or social origins may then influence the further evolution of any or all of those domains.

To explore the many aspects of negative symptoms various approaches are necessary. In spite of the advances made in developing rating scales (Andreasen, 1982), such ratings may not tap underlying psychological processes adequately. More intensive and extensive exploration is also essential. For example, Bouricius (1989) reports an instance in which her son had been diagnosed as having schizophrenia and was viewed as having flat affect at a time when his appearance and behaviour were dull and apathetic. At the same time, however, he was writing very emotionally charged poetry. Noting associations between negative symptoms and the psychological and social contexts in which they emerge can help prevent naive interpretations from brief descriptive reports and provide important clues to psychological processes that might contribute to the generation of the symptoms (Strauss & Hafez, 1981; Strauss *et al*, submitted for publication). Thus this exploration suggesting that negative symptoms are often responses to difficult psychological and social situations uses more detailed description of patients' reports and contexts than is found in traditional symptom ratings.

Possible psychological and social sources of negative symptoms

Reports of patients from our own intensive studies (Strauss *et al*, 1985), reviews of first-person accounts (*Schizophrenia Bulletin*, 1987), and clinical experiences suggest several specific psychological and social contexts in which negative symptoms often arise. These sources suggest ten different kinds of situations that may contribute to these symptoms. The following is a list of these situations with illustrative examples.

1. The pain of relapse into positive symptoms

A schizophrenic patient considered by his psychiatrist to have an 'anhedonic syndrome' described in an interview with one of the investigators (JS) a sequence of factors occurring in his illness. This young man had been a motorcycle racer. He then started developing schizophrenia with delusions of persecution and threatening auditory hallucinations. When he was engaged in motorcycle racing, especially if he were close to winning, these symptoms would become unbearably intense. The patient described this as such a horrible experience that he finally gave up motorcycle racing entirely, an activity that had been one of the few pleasures of his life.

2. *The loss of hope and self-esteem*

One person seen in our intensive longitudinal study who had a history of 12 years of schizophrenic disorder had sunk drastically in quality of life during and between his psychotic episodes. Before the onset of his illness, he had been a highly skilled craftsman. He had been married with one child and was involved with his mother and siblings. Over the years however, he was repeatedly admitted to hospital. When he was able to work, it was as an unskilled labourer. He was divorced, out of touch with his child, and lost contact with other family members as well. He had no friends. How many people could maintain motivation and involvement under such a decline? But somehow, this patient had kept trying, although more and more feebly.

Most recently, he had been admitted to hospital with yet another psychotic episode. In the subsequent 3 months, although still slightly apathetic and withdrawn, he improved gradually and had started to become more autonomous. When noting in a research interview that he had improved, he added: 'I'm almost afraid to think about it. How long will it be until the next time?' Given this attitude, it is perhaps not too surprising that when seen in a follow-up interview 1 month later the subject had withdrawn further. He had been spending most of his time in bed and had been advised finally by his clinician that he should apply for disability payments and would probably not be able to return to work.

3. *The possibility of impulsive or bizarre behaviour*

Negative symptoms may arise when the patient has had problems acting impulsively or acting bizarrely. In some instances it appears as though massive apathy and withdrawal are mechanisms for avoiding such socially or personally destructive behaviours by damping down overall behaviour. In psychotic states, when fine control of action and thinking is severely compromised, a massive withdrawal might be the only way in which display of bizarre behaviour and thoughts, or actual destructiveness, can be avoided.

4. *Problems in finding a new identity as non-patient*

Another situation in which negative symptoms may arise is when the patient confronts the difficulties of needing to find an identity that is not one of being sick. An example of the intensity of this problem was given by one subject in our intensive longitudinal study. This subject has improved considerably over the last several years and was now confronting this issue. She had not developed negative symptoms, but reflected how much she was tempted to give up and withdraw. This young woman wondered during a follow-up interview whether she was going 'crazy' because as she had become better she was losing the structure of her life that had been provided by her illness. She was no longer in treatment other than receiving low-dose neuroleptic medication. She did not want to associate with other patients or former patients. On the other hand, people that she had known prior to her illness now had families and jobs. Having neither, the subject felt out of place with them. In addition, she was perplexed as to how she was going to function in the world as a 'normal'. With these concerns and the feelings they generated, she wondered whether she was going crazy again. Other subjects described being sick as an occupation in itself — a full-time career. One subject told us how difficult it was to give up being sick with its constant self-focus. This subject, like the other, also stated that being sick provided an entire framework for relating to others and receiving help from them.

5. *The feeling of guilt for past dysfunction*

One mother (DuVal, 1987), who had had repeated psychotic episodes, described poignantly her vague awareness during these episodes that they were harming her child who witnessed them. Often people with schizophrenia describe the guilt they feel at being unable to perform in the roles in which they have previously taken pride and also from the actual psychological or physical harm they might have done to their loved ones during the psychosis. During the process of improvement with its increasing awareness of environment, these realisations create for patients a further burden and a pressure to withdraw and give up.

6. *The potential threat of entering complex stressful social situations*

For many patients, particular kinds of social and occupational situations may be extremely stressful, possibly even contributing to symptom recurrence. Interpersonal closeness, for example, is often extremely difficult for some persons with schizophrenia. Negative symptoms may arise from fears of such situations. The symptoms may be reinforced and maintained by also providing a mechanism for avoiding the threat or even the possibility of such a relationship.

7. *Situations where the person is rendered helpless from the disorder, from environmental features, or both*

Persons with schizophrenia may find all their paths to improvement blocked. This may be especially true for people with repeated psychotic episodes who come from low socio-economic classes, have few skills, and are isolated from family and friends. Here, too, there may be the possibility of secondary benefit from negative symptoms. As Schmale has pointed out in another context (Schmale, 1964), giving up under overwhelming conditions may not be as maladaptive as it seems. Giving up at least offers the possibility of recruiting help from others in the social context if such help is available at all.

Three environmental contributors to negative symptoms

Beyond the negative symptoms possibly arising from the person's experience with the disorder itself as described above, these symptoms may also be associated with the following specific social-environmental characteristics.

8. *Institutionalisation*

Behaviours reflective of negative symptoms associated with long-term institutionalisation have been discussed in detail by other authors (e.g. Barton, 1959; Wing, 1962; Goffman, 1961).

9. *The social benefit system*

Although helpful for some, benefit systems sometimes punish patients who attempt to recover. As is so often true, one can see the situation facing a person about to improve by observing someone with schizophrenia who does not have negative symptoms and thus encounters the problems. One of our subjects, a 23-year-old woman with a 6-year history of psychotic symptoms, was able to work her way through college and part way through graduate school. She did this while at the same time working full-time at a skilled job. She accomplished such feats in spite of recurring symptoms and the side-effects from her psychotropic medications. However, because she then began to earn a modest salary, she was no longer eligible for welfare benefits. In addition, she had to pay for her own medications and treatment. As a result, she remained constantly in debt while only being able to support herself slightly above a poverty level. As she got better, she was thus far worse off materially and financially than she had been when she received disability benefits.

10. *The stigma of schizophrenia*

Stigma (Scheff, 1981) is a social situation that seems likely to contribute with particular power to the development of negative symptoms. Such an evolution is consistent with the concept of secondary deviance (Lemert, 1967), the reaction people often have to being viewed as defective, in this case as a mental patient. The reaction to being stigmatised often includes the acceptance of the role and loss of other strengths. This sequence may be influenced by many things including the intensity of the stigma, the severity or chronicity of the disorder, personality traits of the person, and pressures and supports of society.

Beyond these ten psychological and social situations, as further evidence for the hypothesis that psychological and social factors may be sources of negative symptoms, it is important also to note environmental situations that appear to reduce these symptoms. The helpful roles of modest increases in interpersonal contact or useful occupation have been discussed in many reports (Wing, 1962; Breier & Strauss, 1984). More striking changes in environmental situations may also have a salutory effect. There are many reports of withdrawn chronic schizophrenic patients who take leading roles in rescue operations during a flood or a fire, helping save other patients or even helping to organise the general rescue procedures. Only slightly less dramatic are the more systematic reports (Clark, 1988) describing how chronic schizophrenic patients participating in a challenging, engaging activity like a canoe trip begin to communicate, relate to each other, show pleasure, and take an increasingly active role in the venture. Characteristics of novelty, challenge, interpersonal support, trust, and free choice seem to be key factors in such situations.

The psychological and social impacts of negative symptoms on course of disorder

One of the most striking aspects of negative symptoms has been their prognostic power. This has been shown in several large-sample short-term studies (Strauss *et al*, 1974). It has also been found to a lesser extent in at least one carefully conducted long-term follow-up (Harding *et al*, 1987*a*). What is the mechanism for this prognostic effect? One possibility is that negative symptoms contribute to poor prognosis by cutting the person off from potentially helpful environmental resources. Although negative symptoms may help patients avoid or cope with certain aspects of their life situation, these symptoms may also generate positive feedback mechanisms that maintain or exacerbate the disorder with its dysfunction (Strauss *et al*, 1985). There is evidence, for example, that in several mental disorders work and social relationships may prevent decompensation or help people improve (Brown & Harris, 1978; Henderson, 1981; Breier & Strauss, 1984; Strauss *et al*, 1981). Negative symptoms usually undermine functioning in these life contexts. Patients who are too withdrawn to work, who are too apathetic and without affect to form social ties, cut themselves off from the very sources that could provide motivation, structure, hope, material assistance, and advice. Furthermore, vocational rehabilitation programmes often systematically exclude persons with low motivation. Even the treatment system may give up on the patient with negative symptoms, making fewer resources available.

Discussion

Why are negative symptoms so important in schizophrenia when there are so many other disorders that also engender despair, fear of recurrence, and similar problems? One possible answer is the severity of the stigma with which society, (including the patient) views schizophrenic disorders. The diagnosis of schizophrenia is almost unique among mental disorders in terms of the despair that it evokes. For example, a young woman in one study (Rakfeldt, 1987) noted that because she was in hospital with an eating disorder her friends would accept her more than if she had been diagnosed as having schizophrenia. Another study subject (with the diagnosis of schizoaffective disorder) said almost desperately how important it was that he convince the hospital staff that he was depressed, not schizophrenic. He seemed driven to prove to himself and to others that he was not a 'nut' or a 'hopeless case'.

The contributions of treatment interventions to apathy and withdrawal may also be particularly powerful in schizophrenia. Some of the most common treatment efforts may inadvertently create the opposite effect from the ones intended. Patients with schizophrenia are often told that they have a disease like diabetes. They are told that they will have the disease all their lives, that it involves major and permanent functional impairment, and that they will have a life-long need for medication (Harding *et al*, 1987*b*).

One person participating in a workshop on schizophrenia for professionals, consumers, and family members reported that after having received this message she gave up her teaching career. A few years later, a friend advised her instead: 'Try to do a little something — little by little'. She took the advice and started working part-time. The patient, who was still psychotic, found that she was better able to control her psychosis while working. She then became more involved with the world, and began functioning more competently, finally returning to a teaching job. She had surmounted the withdrawal apparently fostered by the well-intended 'therapeutic' intervention.

Finally, the accumulation of undermining experiences may be particularly powerful in schizophrenia. Stigma, discouraging 'therapeutic' messages, social dysfunction, and the problems schizophrenia often generates in functioning cognitively may all interact over time to make remaining engaged, involved, and hopeful particularly difficult.

But could not experiences such as those described above be assumed to be adequately covered by some general term like 'demoralisation'? Perhaps, but such terms in psychological domains are often used as pseudo-explanations to note and de-emphasise the phenomenon in order to make way for detailed biological inquiry. This is similar to how the term 'constitutional factors' was used as a biological pseudo-explanation not so long ago to 'get that out of the way' so the 'really important' psychological features could be explored in detail. Both tendencies are unfortunate. Just as the various possible biological contributions to negative symptoms need to be explored in detail, so too the various psychological and social sources need to be clarified. Only through such a combined approach will be it possible to achieve optimal understanding and treatment.

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Psychological Treatments for Negative Symptoms

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The subject matter of this paper is the psychological treatment of negative symptoms. However, before embarking on a review of the available literature, it is worthwhile considering some conceptual issues and distinctions which are relevant to research in this area.

A useful framework for a psychological perspective on negative symptoms has been proposed by Wing (1975) (see also Wing, this volume), who suggested that schizophrenic impairments fall into three major categories, namely: (a) 'intrinsic' impairments, which are fundamentally biological in nature and involve the symptoms of schizophrenia (both positive and negative); (b) 'secondary' impairments which may be defined as, 'Personal and social reactions to the fact and circumstances of illness, both by the patient and important others'; and (c) 'extrinsic' impairments which consist of vulnerability factors such as low intelligence, personality problems, social and sexual problems, poor education, etc. From a temporal viewpoint Wing was suggesting that 'extrinsic' factors determine the individual's predisposition to breakdown, 'intrinsic' factors the signs and symptoms of illness once a breakdown has occurred, and 'secondary' factors the consequences of the illness in its relationship to the social environment.

Subsequent to Wing's proposal, an important model of psychosis has been proposed by Crow (1980) and operationally defined by Andreasen (1981). This model involves a distinction between 'positive' (hallucinations, delusions and thought-disorder) and 'negative' (flattening of affect, poverty of speech, loss of drive, etc.) symptoms. Although the scientific validity of this dichotomy has not gone unquestioned (particularly with respect to the question of whether negative symptoms are a unitary or a multifactorial phenomenon, cf. Lewine, 1985) it is clearly useful with respect to describing psychotic symptoms and the treatments that might be applied to them.

Putting these two frameworks together, it would seem that psychological interventions with psychotic patients have in particular been directed at intrinsic impairments (both positive and negative) and the secondary impairments that are consequent on these symptoms. This is certainly true of the treatment approaches to negative symptoms, which we will describe in terms of their chronological order and which therefore reflect the development of psychological ideas and approaches over time. The five approaches to be considered are: (a) token economies; (b) social skills training; (c) life skills training; (d) self-instructional training; and (e) problem-solving.

The token economy

The value of behaviour modification in the training of psychotic patients was extensively explored in the late 1950s and early 1960s, particularly in North America (Ullmann & Krasner, 1965). This approach used the principles of operant conditioning which were applied both to individual patients and also to whole wards of patients. The latter group application came to be known as the 'token economy' approach (Ayllon & Azrin, 1968).

The basic idea of the token economy is to motivate patients to behave appropriately and constructively by giving them tokens whenever they behave in an acceptable manner. These tokens can later be exchanged for a number of different reinforcers, which might range from cigarettes, drinks or watching television to permission to sleep in a pleasant single room.

Token economy regimes were introduced into large psychiatric hospitals in the USA in the 1960s with fairly dramatic results. In the early 1970s they began to be used in the UK and produced good but perhaps not quite so impressive results. Token economies appear to be particularly useful with long-stay, chronic, institutionalised patients and their major impact appears to be on negative symptoms. However, the efficaciousness of token regimes does not seem to be dependent on the contingency between tokens and behaviour but rather appears to be a consequence of changes in the way that staff interact with patients (Baker *et al*, 1977). It is important to note that, like other behaviour modification programmes, token systems work best when patients are explicitly instructed about the contingencies at the outset, and the failure to do this has been cited as a major reason why token systems sometimes fail to work (Kazdin, 1977).

Token economy programmes are still thought to be useful, particularly within the context of attempting to transfer long-stay patients from institutions into the community. They do, however, raise a number of problems which include the following: (a) the need to select a relatively homogeneous group of patients; (b) the need to select, train and keep high-calibre nursing staff; (c) the need for a favourable staff-patient ratio;

(d) the need to have the overwhelming support and commitment of all hospital staff from all relevant staff groups; and (e) the need for every staff member to subscribe to a common set of objectives. A further problem posed by token systems concerns their ethical acceptability, as some token regimes require patients to 'earn' reinforcers which are usually regarded as theirs by right (Karasu, 1981).

Social skills training

The major problem underlying most of the negative symptoms is a lack of social skills. Thus, in the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982) three of the five types of negative symptoms considered, concern behaviours which are social in nature (i.e. affective flattening, anhedonia-asociality and attention), while the other two involve personal behaviours which could also relate to the social context.

It is not surprising therefore that social skills training (SST) has been seen as a useful approach with psychotic patients. Unfortunately, such studies that have been undertaken and reported have demonstrated only short-term benefits from SST. Questions remain concerning the durability and generalisation of the improvements achieved (Curran & Monti, 1982).

Life skills training

The training approach to the problems of long-term patients, particularly those presenting negative symptoms, has been extended to encompass not only social but also other skills which are necessary for daily living. An example of a life skills training approach for chronic schizophrenic patients was described by Brown (1982). The programme was carried out in a day-patient unit and lasted for 7 weeks on a 5 days a week basis. The seven training modules involved focused on: (a) interpersonal skills training; (b) nutrition and meal planning (two modules); (c) health and hygiene; (d) managing money; (e) pre-vocational issues; and (f) the use of community resources and social networks.

The major feature of this programme was the emphasis on teaching or training as opposed to treatment. Thus, for example, instead of simply telling patients to take their medication, psychiatrists gave lectures and seminars to groups of patients about the value, and possible side-effects of their drugs.

The initial outcome of this programme was favourable (Brown, 1982) but the longer term effects of life skills training are unknown. However, the conceptual framework of the life skills approach provides an innovative model of treatment which holds considerable promise for the future.

Self-instructional training

One of the most promising innovations in psychological treatment in recent years has been the development of cognitive-behaviour modification techniques. The distinctive feature of this approach is that, unlike earlier behavioural approaches which were narrowly tied to animal research, cognitive-behavioural techniques take into account the patient's capacity to plan and regulate his or her own behaviour (Lowe & Higson, 1981). It might be thought that such approaches hold particular promise for patients suffering from negative symptoms who find it difficult to initiate and control their own actions.

Perhaps the simplest cognitive-behavioural treatment is self-instructional training (SIT), which involves teaching patients to plan and control their own behaviour, first by instructing themselves out aloud and then by instructing themselves covertly (i.e. silently). Meichenbaum & Cameron (1973) first used SIT to improve the performance of schizophrenics on various cognitive tasks and to reduce psychotic speech. However, subsequent studies have called into question the extent to which the gains achieved following SIT generalise. Bentall *et al* (1987), in a series of three experiments, confirmed that SIT could be used to bring about improvements in the cognitive performance of patients suffering predominantly from negative symptoms but little improvement was observed on generalisation tasks, even when attempts were made to teach problem-solving self-instructions that might maximise generalisation. The difficulties observed with respect to generalisation suggest that the efficaciousness of SIT and other similar cognitive-behavioural techniques might be enhanced if they could be tailored to the specific cognitive deficits of particular patients. SIT, as it has so far been applied, assumes a simple lack of self-directed 'inner' speech. This may be an oversimplified view of the cognitive deficits involved in negative symptoms.

Problem solving

Given that patients exhibiting negative symptoms tend to have difficulty in both initiating responses (e.g. poverty of speech, lack of affect) and in organising their behaviour (e.g. speech disorganisation, incongruity of affect) it is of some importance that a recent study of psychotic symptoms demonstrated separate factors corresponding to these two types of deficits (Liddle, 1987). Both of these types of problem are important in the area of interpersonal relationships and it is interesting to note that the distinction between two corresponding classes of social difficulty emerged in an earlier study by Wing (1961). This study used the Wing Ward

Behaviour Rating Scale and demonstrated that the social behaviour of long-stay schizophrenic patients separated into two components: (a) a social withdrawl component reflecting problems in initiating and responding to social contacts; and (b) a factor of 'socially embarrassing behaviour' reflecting problems in organising behaviour with respect to norms of social conduct.

Recent approaches to the social difficulties of long-stay patients, particularly those exhibiting negative symptoms, have adopted a 'problem-solving' approach (e.g. Wallace & Boone, 1983; Hansen *et al*, 1985). These approaches have been influenced both by the growing interest in cognitive approaches to psychopathology alluded to above and by the observation that effective interpersonal problem-solving is related to the number of close friendships and the degree of family support available to discharged patients (Mitchell, 1982).

Hansen *et al* (1985) reported a study carried out with seven chronic psychiatric patients (six with a diagnosis of schizophrenia) who were trained in a procedure for solving interpersonal problems. The procedure involved five steps which were: (a) problem identification; (b) goal definition; (c) solution generation; (d) evaluation of alternatives; and (e) selection of the best solution. Hansen *et al* found that this approach produced positive effects which generalised to non-training problems. The benefits of training were found to persist at 1- and 4-month follow-ups.

Summary and conclusions

Psychological training programmes for patients presenting with negative symptoms have developed from an environmentally based approach (the token economy) through interactive programmes (social and life skills training) to programmes which focus directly on facilitating and enhancing the cognitive skills of the individual patient (self-instructional training and problem-solving). It is clear that this sequence of research has generated a range of approaches which are probably undervalued in the management of patients suffering from negative symptoms. Problems remain with respect to the generalisation of some procedures but it seems likely that these problems may be overcome by tailoring treatments to the particular cognitive deficits of different groups of patients. This will obviously require a detailed analysis of the structure of negative symptoms and the deficits associated with them. The distinction between difficulties in initiating behaviour and difficulties in organising behaviour may prove to be particularly important in this respect.

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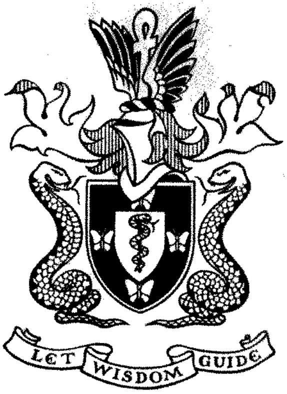

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British Journal of Psychiatry (1989), **155**, 735–738

Annotation

Psychiatric Manifestations of Frontal Lobe Tumours

M. A. RON

In a recent article in the *British Medical Journal* Maurice-Williams & Dunwoody (1988) reported two patients with frontal meningiomas who presented initially to psychiatrists. The correct diagnosis was made in one of them after prolonged, perhaps unnecessary, psychiatric treatment. In the other the diagnosis was made at autopsy. In this case psychiatrists were only briefly involved and neurosurgical referral had been made promptly. The authors, who treat these reports as a cautionary tale, conclude by warning psychiatrists to pay special attention to a number of features in the history and examination of psychiatric patients. In particular we are told that suspicion should arise in the presence of gradual non-remitting symptoms such as irritability, memory loss, self-neglect, dysphasia or incontinence in patients without a previous history of psychiatric disease or clear precipitating factors. They also suggest that we pay attention to the views of relatives when they feel the patient suffers from a physical rather than a psychiatric illness, and emphasise that early diagnosis leads to easier surgical removal and better outcome.

Similar reports have previously appeared in the literature and nobody would deny that this is sound clinical advice. On the other hand, it is also important to guard against unnecessary and costly investigations which are unlikely to disclose brain pathology in all but a very small proportion of psychiatric patients. The purpose of this annotation is to consider in some detail the psychiatric manifestations of intracranial, and in particular frontal lobe tumours, the frequency with which they might occur, and the ways they can present to psychiatrists.

The psychiatric manifestations of intracranial tumours

The clinical manifestations of intracranial tumours are determined by the damage or distortion they cause to structures in their vicinity and by the generalised effects of raised intracranial pressure. It follows that some of these features, including psychiatric symptoms, would be common to tumours of different histological types and localisations. Psychiatric manifestations have been reported to occur at some time in half of the patients with intracranial tumours (Hecaen & Ajuriaguerra, 1956). Mental abnormalities can be divided into three broad categories and the description which follows is largely taken from Hecaen & Ajuriaguerra's (1956) classic monograph.

Approximately a third of the patients experience *confusional states* or *progressive intellectual deterioration*. Disorientation with variable clouding of consciousness, indifference to the outside world, euphoria, childishness, and loss of insight are prominent in those with confusional states, while memory disturbance, loss of initiative, bradyphrenia, and bradykinesia are present in those with progressive intellectual deterioration. Papilloedema and other signs of raised intracranial pressure are particularly common in this group and the syndrome is more frequent with tumours involving both hemispheres. A further 20% experience *behavioural and mood disturbances*. Irritability and euphoria with mild psychomotor abnormalities are the commonest symptoms. Depression, hysterical conversion, and paranoid ideas are less frequent. A smaller number exhibit *paroxysmal disturbances* such as poorly formed visual hallucinations and automatisms, which probably indicate involvement of the temporal lobes. Fluctuations in the severity of mental abnormalities are commonly observed within a progressively deteriorating course, and in many cases symptoms from these three categories coexist in the same patient.

Symptoms of confusion and/or dementia are commoner with frontal lobe tumours followed by tumours in the temporal and parietal lobes, and the same applies to mood and behavioural disturbances. Psychiatric manifestations are far less common with infratentorial tumours and in Hecaen & Ajuriaguerra's (1956) series they occurred in approximately 12% of patients. They also reported a greater frequency of mental abnormalities in patients with gliomas (60%) compared with meningiomas (42%) and other space-occupying lesions, and this is undoubtedly due to the greater speed of growth and destructiveness of the more malignant tumours.

The psychiatric manifestations of frontal lobe tumours

The frontal lobes can be divided into two main components: the motor–pre-motor area, and the pre-frontal area. The latter comprises the paralimbic cortex located in the infero-medial part of the frontal lobe and the heteromodal association area placed in the most anterior part of the lobe. Damage to the motor–pre-motor area results in limb weakness, incontinence, akinesia, mutism, apraxia, and Broca's aphasia, while lesions in the pre-frontal areas result in predominantly mental disturbances, the so-called 'frontal lobe syndrome'. Mesulam (1986), in his excellent review of the behavioural affiliations of the pre-frontal cortex, has pointed out the common thread that runs through the behaviour of these patients. Thus, attentional deficits, shallowness and impulsivity of thought and affect, and the preferential vulnerability of types of behaviour that lack external control are the hallmarks of the syndrome. In clinical practice these deficits have protean manifestations, but in a given individual the localisation, size, type, and course of the lesion will determine the clinical manifestations, which in turn will be coloured by the previous personality and age of onset. In general terms, orbitofrontal and anteromedial lesions are said to produce predominantly affective symptoms, while impaired reasoning and lack of mental flexibility follow dorsolateral ones. In the case of space-occupying lesions symptoms of raised intracranial pressure and those resulting from damage to neighbouring structures (e.g. the motor–pre-motor area) will appear in addition to those of the 'frontal lobe syndrome'.

Frontal lobe pathology often results in profound changes in the personality and behaviour, but at times large lesions can be accommodated with little clinical disturbance and this discrepancy has on occasions led to the delayed diagnosis of treatable pathology. The possibility of frontal lobe tumours presenting with isolated mental disturbances is particularly relevant for psychiatrists. Gautier-Smith (1970) studied 213 patients with parasagittal and falx meningiomas presenting to two neurological centres. Psychiatric symptoms were commoner in anteriorly placed tumours and were the first to appear in over a third of those with anterior parasagittal meningiomas and half of those with anterior falx tumours. Headaches were the presenting symptom in another third and epilepsy in over a quarter. The rest presented with a combination of these features. In those presenting with psychiatric symptoms, impairment of consciousness and progressive intellectual deterioration were commonest, followed by mood and behavioural disturbances which rarely occurred in the absence of intellectual impairment. Neurological abnormalities, such as paroxysmal headaches, epilepsy and unilateral limb weakness, were usually present at the time of diagnosis even in those with early psychiatric symptoms. Incontinence, frequency and urgency of micturition were also seen in these patients. A specific association of disturbances of micturition with frontal tumours was found in 14% of a consecutive series (Maurice-Williams, 1974), and contrary to common belief, the patients were distressed by their presence. The correct diagnosis, even in those presenting with psychiatric features, tends to be made early. In Gautier-Smith's (1970) series only a few patients had experienced psychiatric symptoms for more than two years, and with the use of new imaging techniques the delay in diagnosis is likely to be shortened further. Thus in Chee *et al*'s (1985) study over half of the patients had been correctly diagnosed less than a year after insidious intellectual impairment was first noticed.

How often are frontal lobe tumours misdiagnosed as psychiatric illness?

Anecdotal reports originating from psychiatric hospitals have described patients with frontal lobe tumours in whom psychiatric symptoms had been present for many years before the correct diagnosis was made. Hunter *et al* (1968) described three patients who had been ill for 3, 25, and 43 years. Dementia was prominent in two of them while the third, with the longest history, had florid delusions and hallucinations. In these patients the psychiatric symptoms were accompanied by epilepsy, incontinence, and eventually by signs of raised intracranial pressure. However, such occurrences, like the report which has prompted this article (Maurice-Williams & Dunwoody, 1988), are probably very infrequent.

Much of the evidence suggesting that cerebral tumours may be misdiagnosed as psychiatric illness accrues from post-mortem studies carried out in mental hospitals. These studies, published long before modern imaging techniques had become available, are unlikely to reflect the current frequency of such misdiagnosis. In one of the most comprehensive studies sampling several North American psychiatric hospitals (Morse, 1920), the prevalence of intracranial tumours, a third of which were frontal, was between 1.3% and 2.6%. Over a third of the patients were either mentally subnormal and had entered the hospital many years previously or had long-standing psychosis before symptoms attributable to the tumour became apparent. In such cases, it seems unlikely that the neoplasms were responsible for the psychiatric disturbances, although they may have aggravated or modified them at a later stage. This point has recently been emphasised by Law (1988), who quotes an annual incidence of 6.6 per 100 000 of primary tumours of the central nervous system in the UK. Given the high overall incidence of psychiatric illness, the chance occurrence of both conditions in the same patient is to be expected.

More up-to-date information on the prevalence of intracranial tumours in psychiatric populations can be obtained from some recent studies using computerised tomography (CT). Larson *et al* (1981) surveyed retrospectively 123 psychiatric patients who had undergone CT to exclude the presence of brain pathology suspected on clinical grounds. Three patients were found to have brain tumours, one of them frontal, and a further three had subdural haematomas. All six patients had neurological abnormalities on examination, while this was not the case for those with normal CT. The high frequency of neurological abnormalities in this series suggests that the prevalence of brain pathology is likely to have been considerably higher than in unselected psychiatric populations.

More recently Roberts & Lishman (1984) have reported the results of the CT scans in 323 patients examined at the Maudsley Hospital over one year. Some of these patients were scanned to exclude the presence of clinically suspected brain pathology, while others were patients suffering from major psychoses or alcoholism investigated for research purposes. Ventricular and sulcal enlargement were the commonest CT abnormalities. Only one patient in the series had a brain tumour, a parieto-occipital astrocytoma. Three others had infarcts or intracerebral haematomas. In most cases, brain pathology had been suspected because of the previous occurrence of 'organic' events (e.g. head injuries, epilepsy, etc.) or because of neurological abnormalities. As a result of the study the diagnosis was changed from 'functional' to 'organic' in two cases and in most patients the CT findings did not lead to new therapeutic approaches.

The prevalence of intracranial neoplasms varies depending on the psychiatric diagnosis. In the Morse (1920) series, intellectual decline and impaired consciousness were the main features in those in whom the neoplasm was likely to have been the cause of the mental abnormalities. Intracranial tumours have also been found in patients undergoing investigations for dementia, although frontal lobe tumours do not appear to be over-represented in these studies. Before CT, Marsden & Harrison (1972) found eight space-occupying lesions, none of them frontal, in the 106 patients referred to them with the presumptive diagnosis of dementia. A similar proportion of tumours, in this case gliomas in unspecified locations, was detected by Victoratos *et al* (1977) using pneumoencephalography, and by Smith & Kiloh (1981), one of whose patients had a left frontal astrocytoma. Using CT, Jacoby & Levy (1980*a*) found a corpus callosum tumour and a right frontal subdural haematoma in a group of 40 elderly demented patients. The need to investigate dementing patients does not need to be emphasised here, but the detection and removal of intracranial meningiomas has frequently lead to substantial clinical improvement even in those with long-standing symptoms (Chee *et al*, 1985).

The association between intracranial tumours and schizophrenia is less close. Psychotic symptoms were rare in the Morse (1920) series, and Davison & Bagley (1969), in their review of previously published cases, suggest that while the incidence of schizophrenia may be increased in patients with temporal and pituitary tumours, this is not the case with those located in the frontal lobes. In a group of 268 patients examined during their first episode of schizophrenia, Johnstone *et al* (1987) failed to find intracranial neoplasms in the 15 who had organic brain disease considered relevant in the causation of the psychiatric symptoms. Frontal pathology was also rare in the series of chronic schizophrenics reported by Owens *et al* (1980) who discovered unsuspected intracranial lesions in 12 of 136 patients using CT. Three of them had frontal or fronto-parietal infarcts which probably occurred many years after the onset of their illness and a fourth had a left frontal meningioma. This patient, a woman in her 70s who had been first admitted to hospital ten years previously, had a positive family history of schizophrenia and had responded well to phenothiazines. Her refusal to undergo surgical treatment made it impossible to unravel the link between the two conditions.

Intracranial tumours appear to be equally rare in patients suffering from strictly diagnosed affective illness and in whom the neurological examination was also normal. Thus Jacoby & Levy (1980*b*) did not find any tumours in 40 carefully selected elderly depressives who had undergone CT, and the same was the case in 108 younger patients investigated by Dolan *et al* (1985).

Conclusion

Occasional reports of psychiatric patients who are found to have brain tumours, perhaps more often in the frontal lobes, have appeared in the literature for many years and may continue to do so from time to time. Failure to make the correct diagnosis has serious implications, as early surgical treatment carries a better prognosis. However, to perform costly investigations for every psychiatric patient because of the rare chance of finding a brain tumour is unnecessary and wasteful. In this age of advanced technology, a detailed clinical history and a careful physical examination are still the best predictors of brain pathology. For the patient with a suspected brain tumour, CT using enhancement is the investigation of choice, although magnetic resonance imaging (MRI) provides a superior visualisation of lesions in the posterior fossa. Other investigations such as electroencephalography are far less sensitive and should not be relied upon to exclude the presence of a brain tumour.

In terms of psychiatric diagnoses, patients suffering from strictly defined schizophrenia or affective illness are unlikely to have intracranial tumours if neurological symptoms and signs are absent, and the same applies to those with more clearly 'neurotic' symptoms. The search for brain pathology in these patients is bound to prove fruitless. On the other hand patients with intellectual deterioration, impairment of consciousness, unexplained personality changes of the 'frontal lobe' type, incontinence, or suspected raised intracranial pressure should be thoroughly investigated. Finally, we need to remember that intracranial tumours and other brain pathology may appear in patients with primary psychiatric illness and that it is necessary to keep the neurological status of chronic psychiatric patients under review.

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Review Article

Deinstitutionalisation — from Hospital Closure to Service Development

GRAHAM THORNICROFT and PAUL BEBBINGTON

The necessary components of a comprehensive service of local non-institutional forms of care for the seriously mentally ill have been researched separately in pilot trials, but not within integrated programmes for defined populations. Reported outcomes are at least as favourable as for traditional long-term hospital care, but alternative provisions are no less costly. A case manager system may allow co-ordinated formal and informal services to meet the individual needs of chronically ill patients. Poorly integrated programmes will expose discharged patients to disadvantages.

The recent history of the treatment of those with severe and chronic mental illness must be one of the most significant social changes of our time. It has hardly gone unremarked, but it is typically an area in which informed opinion has had scant effect on the underlying policies or on their implementation. This seems tragic in view of the major impact that the change has had on the lives of tens of thousands of people, both patients and their relatives who are increasingly faced with the burden of care. In this paper, we chart the current rush from hospital towards community care and the work that has attempted to evaluate the process. Although the processes of deinstitutionalisation and of the development of alternative community services vary between countries (Mangen, 1988), there are common themes which we shall try to identify in this paper. In doing this we have drawn mainly on the extensive British, American and Italian literature.

Definitions

Deinstitutionalisation has been succinctly defined by Bachrach (1976) as the contraction of traditional institutional settings, with the concurrent expansion of community-based services. We will use this distinction to describe the components of these processes, which may be related more in hope than practice. Brown (1975), the then Director of the National Institute of Mental Health, identified a further essential component of deinstitutionalisation: the prevention of inappropriate mental hospital admissions. Another important distinction is that between asylums as institutions and asylum as a function: the provision of a place of safety or haven is not necessarily related to institutional size (Wasow, 1986; Rosenblatt, 1984; Wing & Furlong, 1986; Goldman *et al*, 1983*c*). Finally, the term 'community care' requires careful specification. The concept ambiguously implies both care in and by the community, and so has united supporters of the former (libertarian radicals) and the latter (fiscal radicals). It may imply merely a change in the locus of care, or, more thoroughly, in the methods and financing of care delivery (Goldman *et al*, 1983*b*).

Methodological issues

The evaluation of outcome for psychiatric patients after discharge from hospital has been reviewed by Avison & Speechley (1987). They report that six forms of outcome criteria are used in such studies: the hospital readmission rate, the interval before readmission, social role performance, social adjustment, symptom levels and combined global ratings. They found that studies rarely employ a full range of social, clinical, economic and service usage outcome measures, and characteristically use small and heterogeneous samples, with imprecise, poorly validated and inconsistent measures (Hall, 1979, 1980; Schulberg & Bromet, 1981; Goldman *et al*, 1986).

Outcome studies of alternatives to long-term hospitalisation were reviewed more specifically by Braun *et al* (1981) and Kiesler (1982). These reviews included the relatively few studies which at least partially fulfilled the following criteria of methodological adequacy: randomised control design (Newcombe, 1988), clear sociodemographic description, adequate accounts of both the experimental and the control programmes, the use of validated instruments for outcome, and a sufficient number of cases and length of follow-up.

The limits of model programmes

The absence of clearly defined and evaluated programmes of care services for the chronic mentally ill has led to the establishment of demonstration centres of good practice. Bachrach (1980) has provided a valuable corrective to the over-interpretation of findings from these schemes. She defines a model programme as a "planned demonstration effort that tests the application of distinctive, often innovative, programmatic strategies to the care of chronic mental patients". Successful models target chronic patients, link with other resources, and provide a range of individually tailored treatments. There are, however, limits to their general application and replicability, because they employ special start-up funds, enjoy the non-specific 'Hawthorne effects' of being part of an experiment, and benefit from the contributions of charismatic individuals. They may only treat a selected sub-population of patients, and may not be able to sustain their initial enthusiastic momentum. For these reason, the results from each pilot programme must be interpreted with caution.

The process of hospital closure

Trends in services since 1954 in Britain

In Britain, the numbers of in-patients peaked at 148 100 in 1954 (Tooth & Brooke, 1961). On 19 February 1954 Mr Kenneth Robinson introduced a Private Members' Bill to the House of Commons, "That this House . . . expresses its concern at the serious overcrowding of mental hospitals . . . " (Jones, 1972). A reduction in numbers was seen as the only humane option. In the following year Houston (1955) wrote in the *Lancet*, "By incarceration we were aggravating the natural process of the disease. At last a new era is dawning and the doors of despair are being unlocked."

The decline in numbers of psychiatric in-patients has continued at an even rate since 1954 (Thornicroft, 1988). The average number of psychiatric beds occupied each day in 1985 in England and Wales was 64 800 (Audit Commission, 1986). This represents a return to the occupancy level last seen in 1895 (Scull, 1984).

Service trends in the United States

The trend of rising numbers of psychiatric in-patients until the mid-point of the twentieth century has been thoroughly documented (Jones, 1972; Rothman, 1971; Scull, 1979; Levine, 1981; Morrisey & Goldman, 1984; Busfield, 1986). In the United States, for example, there were 8500 psychiatric in-patients in 1860, compared with 535 500 a century later (Castel *et al*, 1982; Scull, 1984). Since then this process of deinstitutionalisation in Britain has been paralleled in the United States. From a maximum in-patient population of 558 900 in 1955, numbers had fallen to 132 164 by 1980 (Scull, 1984). At the peak of this process during the 1970s, the institutional population was diminishing by as much as 6% each year (Mechanic, 1986).

Rationalising hospital closure

The recognition of institutionalism

The justifications for this transfer of long-stay patients from the larger psychiatric hospitals are many and varied, being associated with sociological, financial, pharmacological, administrative and legal changes (Jones, 1972; Hawks, 1975; Scull, 1984; Solomon *et al*, 1986). Both within and without the psychiatric profession a view criticising the ill-effects of prolonged stay within the large institutions emerged with increasing force during the 1950s (Miller, 1985). Barton (1959) described 'institutional neurosis' as "a disease in its own right . . . characterised by apathy, lack of initiative, loss of interest". He confidently asserted that hospital "rehabilitation solves these problems".

Extending this, Goffman (1961) formulated the concept of the 'total institution', central to which was "the handling of many human needs by the bureaucratic organisation of whole blocks of people", so that those admitted are "shaped and coded" into the roles of psychiatric patients. Wing & Brown (1970) reinforced this view with their description of the 'institutionalism' of chronic patients. From their study of long-stay patients in three British hospitals, they accepted "the hypothesis that the social conditions under which a patient lives (particularly poverty of the social environment) are actually responsible for part of the symptomatology (particularly the negative symptoms)", although they stressed that institutionalised practices were not confined to large facilities.

Financial incentives and constraints

Financial considerations have been especially important in the United States in fostering this transfer of care. Since the 1960s federal mental health funding was provided through two mechanisms: categorical programmes and reimbursement. The former consisted of grants-in-aid to state, district, and local organisations for targeted programmes, while the latter were the insurance provisions of Medicaid and Medicare. These forms of reimbursement introduced a perverse bias towards accommodating former in-patients in nursing homes, even when a lesser degree of supervision might be required (Brown, 1985). These programmes did provide, together with Supplemental Security Income (Goldman *et al*, 1981), a safety net of provisions, but they have underwritten a transfer of responsibility from the state to local care providers: the public sector has accepted the main responsibility for the long-term mentally ill, while the private sector offers acute services (Levine, 1981; Sharfstein, 1978; Scull, 1984; Mechanic, 1986).

In Britain, general public expenditure has declined since the early 1970s. Moreover, although psychiatric services were designated as a priority area (Jones, 1988), the share of total NHS spending allocated to them during the last decade has fallen (Bosanquet, 1986). In addition, despite attempts to promote joint financing, only 5% of joint funds have been used for the mental health services (Knapp *et al*, 1987). Recent proposals for local authority social service departments to become the 'lead agencies' in providing community services for the mentally ill (Griffiths, 1988) were made in the context of a total current NHS expenditure on mental health services of approximately £1 billion, compared with £42 million by local authorities (Mahoney, 1988; Marks, 1988). The funding of the psychiatric services generally has reflected wider trends in public sector spending within the last decade: resource control through cash and manpower limits, cost containment through efficiency savings and self-funding, and the centralisation of decision-making (Carrier & Kendall, 1986). It is within this economic climate that cost–benefit analyses have been used increasingly in the evaluation of psychiatric services (Glass & Goldberg, 1977).

Treatment developments

Treatment patterns have also shown rapid change. Within three years of the formulation of chlorpromazine in 1952, its use as an antipsychotic agent was widespread (Jones, 1972). This was paralleled by innovations in patient management. Industrial therapy organisations were set up (Early, 1978; Wing, 1960), therapeutic communities were developed (Jones, 1968; Clark, 1974), day hospitals appeared, hostels and halfway houses were established (Golomb & Kocsis, 1988), and in both Britain and the United States community mental health centres were founded (Levine, 1981; Brough *et al*, 1983).

Legal influences

The legal provisions relating to the mentally ill in Britain were unified in the Mental Health Act 1959. This established Mental Health Review Tribunals, dissolved the Board of Control, and delineated the responsibilities of central and local government (Jones, 1972). In the United States there were also significant legal changes during this period. President Kennedy heralded the 1963 Community Mental Health Centers Act as a "bold new approach" (Levine, 1981). Designated catchment areas serving populations of no more than 200 000 were to be served by Mental Health Centers. The central assumption was clearly revealed in the 1975 Amendment to the Act: "community mental health care is the most effective and humane form of care for a majority of mentally ill individuals".

Hospital inquiries

A series of inquiries into malpractice in British hospitals for the mentally ill provided further critical evaluation of psychiatric institutions. Martin (1984) has documented 14 investigations and inquiries in Britain from 1969 (Ely) to 1980 (Rampton). He set out the recurring themes associated with established cases of ill-treatment: isolation of the institutions, lack of staff support, poor reporting procedures, a failure of leadership, ineffective administration, inadequate financial resources, the divided loyalties of trade unions, poor staff training, and occasional negligent individuals. These influences combined to allow the substitution of secondary aims, such as the establishment of ward routines, for the primary aim of delivering care to patients. The effect of such inquiries was to reinforce the developing view that the large institutions were self-evidently harmful.

Current Government policies in the United Kingdom

British Government policy, as set out in the White Paper *Better Services for the Mentally Ill* (DHSS, 1975), has established a target of 47 900 in-patient psychiatric beds after the completion of the current programme of closure of psychiatric hospitals. On these estimates, 84% of the planned reduction in long-stay psychiatric beds towards this goal from the high point in 1954 has already happened, and only the final sixth of long-stay patients remain to be relocated. Alongside this attrition, there has been a corresponding increase in the annual number of admissions: from 78 586 in 1955 to 185 514 in 1981 (Social Services Committee, 1985; Wilkinson & Freeman, 1986).

Current policies in the United States

Present United States Government policy is embodied in the National Plan for the Chronically

Mentally ill, which codifies the results of the President's Commission on Mental Health (Goldman *et al*, 1981). The chronic mentally ill population is defined by diagnosis, by level of disability and by duration of hospital stay. In practice the disability criterion is most usually taken as met by those patients who are registered as disabled persons and so are eligible for Medical Assistance funds. The numbers of such patients can be estimated from those receiving Social Security Disability Insurance and Supplemental Security Income at state and small area levels (Ashbaugh & Manderscheid, 1985). Of an estimated 1.7–2.4 million chronically mentally ill persons in the United States (Goldman *et al*, 1983*a*), only 116 000 remained within state mental hospitals by 1983 (Bachrach, 1986*a*). A Government review of policy (General Accounting Office, 1977) demonstrated that community-based facilities have been implemented "in the absence of a planned, well-managed and systematic approach". In response to this criticism, NIMH Community Support Programs were established in 1977. Fifteen sites provided demonstration projects of services for chronic mentally ill patients (Scull, 1985). In reviewing the outcome of these initiatives, Tessler & Goldman (1982) saw this programme as "an incomplete reform". They found that the political trend towards shifting responsibility and costs for the chronic mentally ill from federal to state level threatened to undermine the benefit of these federal programmes.

Service developments in Italy

Far-reaching policy changes have been introduced more rapidly in Italy than in Britain and the United States (Mollica, 1985), and allow limited comparisons to be made. Data of the Central Institute of Statistics in Rome show that the number of psychiatric in-patients in Italian hospitals has declined annually since 1963 (Bennett, 1978; Tansella *et al*, 1987; Maj, 1985). Law 180, enacted in 1978, formalised and accelerated this pre-existing trend in the care of the mentally ill (Tansella *et al*, 1987). In the north-western region of Piedmont, for example, there was a fall from 5544 to 2396 psychiatric beds between 1977 and 1981 (Becker, 1985). In contradistinction to the policies in the United States and Britain, the major provisions laid out that no new patients be admitted to the large state hospitals, nor should there be any readmissions after 1 January 1982. No new psychiatric wards or hospitals were to be built. Psychiatric wards in general hospitals were not to exceed 15 beds and must be affiliated to community mental health centres. Community-based facilities would be responsible for a specified geographical area, staffed by existing mental health personnel (Mosher, 1983).

In essence, the legislative reforms have reversed the previous order of priorities accorded to hospital and community forms of service provision (Perris & Kemali, 1985; Tansella, 1986). A number of evaluative studies have appeared in recent years (Rawnsley, 1986). Bollini *et al* (1986) performed a case-control descriptive study of patients in community mental health centres, psychiatric wards in general hospitals, private community facilities, and those remaining in large psychiatric hospitals. The patients remaining in the large institutions had more illiteracy, history of prolonged illness, organic diagnoses, and previous custodial treatment, and had lower expectations of their own social functioning.

At the national level, Tansella *et al* (1987) have reviewed the effects of the reforms on the structure and function of the Italian psychiatric services. As a result of the closure of hospitals since 1978, there had been a progressive decline in the number of public mental hospital beds, to a level of 0.76 per thousand of population by 1983. Secondly, the number of private psychiatric hospital beds had declined by 7% and the total number of patients by 12% in the three years following 1978. In the first two years after enactment, expenditure on community services increased by only 28%, to bring it up to 30% of the total psychiatric budget.

Finally, suicide rates have been examined as one index of psychiatric morbidity before and after 1978. Williams *et al* (1986) compared the trends in suicide rates attributable to mental illness between the periods 1973–77 and 1979–83. The rate was found to have increased consistently over the whole time period, with no clear increase in the proportion of suicides attributable to the legal changes.

The Italian reforms suggest that moving the centre of gravity of psychiatric services from hospitals to community services has been implemented rather slowly and inconsistently. Clear indications have not yet emerged on the adequacy of local services for the younger patients who would have otherwise constituted the 'new long-stay' patients (Mann & Cree, 1976; Becker, 1985).

Target levels for psychiatric services

There is considerable debate about the numbers of psychiatric beds that are necessary (Wing, 1971; Hailey 1971). The 1975 British White Paper suggested targets of 50 District General Hospital beds per 100 000 of the population, together with 35 for the elderly severely mentally infirm and 17 for the 'new' long-stay patients. More recently, the House of

TABLE I

Effects of deinstitutionalisation on the manifest functions of psychiatric hospitals

Function	*Effect of transferring function to community services*
Active treatment for short- to intermediate-stay patients	Function maintained or improved: but data from model programmes may not be generally applicable
Custody for long-stay patients	Function maintained in residential homes: quality of care variable
Physical assessment and treatment	Function may be better transferred to GP
Protection of patients from exploitation	Function markedly impaired: increased physical, sexual and financial vulnerability
Respite for family	Function equivocal: locus of treatment at home, offset by potential for increased professional support to family
Haven/asylum for patient	Function maintained in crisis/foster homes, or impaired in home treatment
Research and training centre	Function partially decentralised: greater co-ordination and flexibility required
Provision of day and out-patient services	Functions decentralised and may be impaired if successor services not established: renegotiation of responsibilities of health and social services for day care. Opportunities to work from health centres
Secure provision for involuntary and assaultative patients	Function vulnerable: clear commitment needed to provide well-staffed units
Occupation and vocational rehabilitation	Function at risk if industrial and occupational therapy not transferred
Shelter, nutrition, basic income and clothing	Functions decentralised and at risk without continuity of care

TABLE II

Effects of deinstitutionalisation on the latent functions of psychiatric hospitals

Function	*Effect of transferring function to community services*
Job security to professional ancillary staff	Function less secure: staff roles, numbers, location, and pay may change
Segregation from society of deviant or dangerous members	Function impaired: behavioural deviance more visible in urban areas
Economies of scale from block treatment	Function vulnerable: dependent upon size of residential settings and staff: patient ratios
Local tax base, and consumer of local goods and services	Function lost: redevelopment of hospital site may offset loss
Segregation within psychiatry of less attractive patients	Function impaired: but two-tier community services may develop
Structured roles and identities for staff and patients	Function eroded: risks of role blurring and patient anonymity
Providing the illusion of comprehensive care	Function reduced: consequences of inadequate care more publicly visible

Commons Social Services Committee report on Community Care (1985) noted that "a smaller number of in-patients beds is now thought necessary for general psychiatric services", and a Royal College of Psychiatrists working party has specified this as 44 acute beds for a population of 100 000 (Hirsch, 1988).

The process of service development

The manifest and latent functions of the psychiatric hospital

A clear understanding of what would constitute an adequate replacement of hospital care for the chronic mentally ill must be based upon a knowledge of the functions served by such hospitals. Bachrach (1976) distinguished between the manifest and latent functions of institutions. The former are those that are intended and recognised by the participants, while the latter are unintended, unanticipated and often unrecognised consequences (Mirabi *et al*, 1985). These manifest and latent functions and the extent to which they can be maintained by community-based services are summarised in Tables I and II.

Analysed in this way it becomes clear that current policies focus almost entirely on the manifest hospital functions. Inadequate attention to the latent functions can provide barriers to the success of the whole programme.

Transitional issues: discharge planning

The selection of patients for rehabilitation has often proceeded in an unsystematic and *ad hoc* manner (Bachrach, 1976; Watts & Lavender, 1987; Falloon & Marshall, 1983). Discharge planning follows such patient selection, and has been shown to be highly variable between psychiatric units (Caton *et al*, 1984*b*). Using a Discharge Planning Schedule, the authors found that drug treatment and psychiatric after-care were the best arranged provisions on discharge for a group of 119 chronic schizophrenic patients, while living arrangements were least satisfactorily planned. Adequate discharge planning was related to improved treatment compliance at three-month follow-up and to a reduced rate of early readmission. The timing and degree of consultation with patients and relatives may also improve outcome (Bachrach, 1976; Shugar *et al*, 1986). Furthermore, in assessing the suitability of in-patients for discharge, both clinical and social disability need to be considered, as these may not be correlated (Wykes *et al*, 1985; Sturt & Wykes, 1987; Brewin *et al*, 1987).

To examine the effect of discharge planning, Linn *et al* (1977) randomly allocated 420 chronic patients from five Veterans Administration hospitals to foster care preparation or continued hospitalisation and followed them up for four months. The experimental group, which excluded severely disturbed patients, showed improved social functioning and adjustment, and 88% had been discharged from hospital.

Principles guiding service development

The Royal College of Psychiatrists (1987), in collaboration with organisations representing psychiatric patients and their families, has set out the principles which should guide the establishment of a programme of local mental health services. They should be comprehensive in meeting the whole range of psychiatric disturbances, accessible geographically and culturally, and acceptable to clients, their families and their neighbours. The interventions should be of proven effectiveness, and must be efficient in cost-benefit terms.

Direct services

Models of residential services

The success of community-based services is crucially related to the nature and availability of accommodation. Within the British context, Wing & Furlong (1986) have described a ten-fold typology of sheltered housing for people with severe psychiatric disorders. The level of least supervision is that of unsupervised housing, in which the individual lives alone or with family or friends. Contact with psychiatric services is through non-residential staff. A variation of this arrangement is to afford a degree of administrative protection, for example from eviction for incurring arrears in rent. At the next level, supervised housing provides regular domiciliary supervision by a mental health practitioner to sustain standards of hygiene, nutrition, and household maintenance (Anstee, 1985). In group homes, which may be arranged in clusters, several residents with psychiatric disorders share the same house, which may be supervised by a residential landlord or landlady, with support from visiting staff.

In supervised hostels, residents may each have a bedroom and share communal facilities, with residential staff offering close daily supervision (Goldberg *et al*, 1985). A higher level of supervision is required for residents more disabled by psychiatric or physical conditions: the hostel model can be supplemented with night nursing staff, the provision of meals, and the supervision of budgeting (Wing, 1982). For those with severe behavioural disturbance, an intensive supervision hostel (or hostel-ward) may be needed, characterised by high staffing levels, a structured regime, a perimeter area, and the rapid availability of extra staff (Garety & Morris, 1984). Finally, a form of basic nursing unit will be necessary for people who are incontinent, immobile or disorientated.

In the United States, these gradations of care have been provided in a range of different settings. A level of support similar to supervised housing is provided in sheltered lodging, or board-and-care homes (Linn *et al*, 1977). These are often privately owned homes or hotels that provide lodgings, meals, and medication management for an unlimited period (Blaustein & Viek, 1987). In 1977 approximately 20% of the two million chronic mentally ill people in the United States were living in such homes (Goldman, 1981). A further variation of this form of hostel is required for residents with severe physical disabilities, and in the United States nursing homes are the most frequently used provision for the elderly chronic mentally ill (Linn *et al*, 1985).

It is argued, both by professionals (Lamb, 1982) and by the users of these forms of accommodation (Casteneda & Sommer, 1986), that a comprehensive psychiatric service must include a flexible range of accommodation, with many levels of professional support varying with the changing needs of each resident.

The facilities described in this section provide primarily for chronic psychotic patients in periods of full or partial remission. Community-based alternatives and methods of crisis intervention are also being developed for the periods of relapse that have traditionally been managed in hospital (Brandon, 1970; Fenton *et al*, 1982; Hoult & Reynolds, 1984; Weisman, 1985) and have received critical attention elsewhere (Braun *et al*, 1981; Tantam, 1985; Marks *et al*, 1988).

The evaluation of residential services

Before turning to the question of how adequately residential services provide for long-term patients after discharge, it is necessary first to ask where the patients are (Johnstone *et al*, 1984). Leavitt (1984) made estimates for the 55 000 patients who would have been in state hospital beds, had deinstitutionalisation not occurred in California. He estimated that 45% were in board-and-care residential homes, 22% were independent or with their families, 7% were in locked facilities, 7% in halfway houses, and 9% were in-patients. The remaining 9% were untreated and mostly homeless. In Britain, Jones (1985) followed up 34 long-stay patients in York for one to two years after discharge. They had been in-patients continuously for more than 12 months before discharge, and 68% had a diagnosis of functional psychosis. She showed that 44% lived largely independently in their own homes, flats or lodgings, and as many lived in sheltered homes or hostels.

Evaluations of differing residential settings have been largely unsatisfactory, either because they were uncontrolled or inappropriately matched, or because residential provisions were only one among many variables in a 'package of care' delivered to discharged patients.

The quality of life of patients discharged to new residential facilities has been reviewed by Lehman (1983). In an uncontrolled study, Lehman *et al* (1982) administered the Quality of Life Interview to 278 randomly selected residents of board-and-care homes in Los Angeles. The respondents were most consistently dissatisfied with unemployment, poverty, housing, and their relationships with friends and family. In an extension of this project, Lehman *et al* (1986) compared quality of life between long-term hospital patients and residents in board-and-care homes. Regardless of their length of stay, the community residents perceived their living conditions more favourably, had more financial resources and were less likely to have been assaulted in the last year.

These findings are supported by a five- to nine-year follow-up study of 120 Feighner-criteria chronic schizophrenic patients discharged from Shenley Hospital in North London (Johnstone *et al*, 1981). In the 66 cases where social information was available, 35% lived with a spouse, 39% with other family members, usually parents, 11% lived alone and 15% in residential accommodation. Although severe emotional, social, and financial problems were commonplace, not one patient in this study sought readmission to hospital, and few relatives favoured this course.

These studies plainly demonstrate the great variation in location at follow-up, with the majority needing continuing supported accommodation. This work also emphasises the need for effective monitoring and tracing systems for relocated patients.

That institutionalism may be independent of the size of the facility has been shown in a West German study of 961 chronic patients in nursing homes, group homes and a state hospital. Kunze (1985) demonstrated that the nursing homes manifested the most impoverished social environment, housed the most chronic and severely disabled schizophrenic patients, and were at least as likely to foster the features of institutionalism as the state hospital (Wing & Brown, 1970).

A considerable concern is that discharged patients will rapidly lose contact with services, in spite of remaining symptomatic or socially disabled. An uncontrolled interview study in Los Angeles of 101 residents of board-and-care homes who had been recently discharged from hospital found that initially over half had contact with community occupational rehabilitation services, but in only a quarter of cases was this maintained (Lamb, 1979). Among the whole group, over half had no goals to change any aspect of their lives (Lamb, 1977). At six-month follow-up a third of the patients had changed their accommodation at least once (Lamb, 1980).

The issue of residential mobility in the North American context was studied by Caton & Goldstein (1984*a*) in Manhattan. One year after discharge, half of the study group of 119 chronic schizophrenics had changed their living arrangements at least once. Typically, different housing placements were arranged after each readmission.

Models of occupational services

The significance of daily occupation is illustrated by the finding of Wing & Brown (1970) in the Three Hospital Study that the amount of time patients spent doing nothing was directly related to their levels of primary symptoms. Occupation may usefully be seen as either work (a purposeful activity requiring effort and discrimination that has a social significance) or employment (an economic exchange relationship where effort is rendered for payment) (Hartley, 1980). Occupation may confer a sense of mastery, through the performance of social roles. It may also bring social status and social contacts. Finally, it can be a criterion of recovery (Shepherd, 1984). Many long-term psychiatric in-patients are involved with occupational therapy, but very few indeed maintain competitive employment (Ford *et al*, 1987).

To respond to this need for occupational rehabilitation, a 'club-house' model of day-centre care has been developed, based upon Fountain House in New York (Beard, 1978). The chronic mentally ill become members of a club that offers a centre where they can drop in for social activities or refreshment. There are also concurrent programmes of vocational training which actively encourage members to participate in the planning and running of the club.

As an extension of the club-house approach, Transitional Employment Programs, also originating at Fountain House (Beard, 1982), are gaining in popularity in the United States. Each Program is an agency that negotiates positions for unskilled labour with local employers, and guarantees that there will be no employee absences. If a Program employee does not attend work, the vacancy is filled immediately from the pool of other workers, or by one of the Program staff (Beard, 1978).

Day hospitals were begun in Britain in 1946 after their establishment in the Soviet Union a decade earlier. They provide a service that can compare favourably with standard in-patient treatment for those in acute relapse (Hirsch *et al*, 1979; Dick *et al*, 1985). Unless, however, day hospitals are specially orientated to the needs of the chronic mentally ill (Archarya *et al*, 1982), such patients are more likely to attend social service day centres, which are less well staffed, and more orientated towards support than treatment.

The evaluation of occupational services

Anthony has reviewed the literature on the specific effects of occupational rehabilitation programmes upon performance outside hospital (Anthony, 1972; Anthony *et al*, 1978). Overall, the proportion of patients who are readmitted increases as the period of follow-up lengthens (Pryor & Distefano, 1986). Five to ten years after discharge, only 25–30% of the patients had avoided readmission. Several treatment variables were indicators of outcome. Day centre attendance was associated with lower readmission rates (Kruzich & Berg, 1985; Dickey *et al*, 1986), as were medication compliance, and contact with psychiatric supervision. Contact with occupational centres is also highly associated with their geographical accessibility (Lamb, 1979).

The continuing need for in-patient facilities

Several authors have described groups of patients whose needs are not and will not be met by acute and community-based services alone (Rachlin, 1976; Bennett, 1979; Bowen, 1979; Talbott, 1984; Harris *et al*, 1986*b*). These are the elderly demented and behaviourally disturbed, the mentally impaired and psychotic, the brain damaged and assaultive, the psychotic and assaultive, and those chronic schizophrenic patients who are vulnerable to neglect and exploitation. Gudeman & Shore (1984) have estimated that there are at least 15 patients per 100 000 population in these categories who cannot be adequately cared for in community facilities. Such patients will continue to require the provision of asylum, whether or not this is provided within asylums (Bachrach, 1986*b*).

The indirect provision of psychiatric services

The influence of patients' and public attitudes

Do long-stay in-patients wish to leave hospital? There is a notable lack of information about this (Weinstein, 1979). Abrahamson's survey (1982) showed that patients with more than ten years of hospitalisation are more likely to wish to remain in hospital, and usually gave realistic reasons. Conversely, patients' attitudes towards hospitalisation may strongly predict their length of hospital stay, and their likelihood of readmission (Drake & Wallach, 1988; Kalman, 1983).

Ambivalent or adverse public attitudes towards the discharged mentally ill may further attenuate the security of former patients (Goffman, 1968; Appelbaum, 1987). The seminal work of Nunnally (1961) on public attitudes towards the mentally ill demonstrated that they were regarded with fear, distrust and dislike by the general public. Their behaviour was seen to be characteristically unpredictable (Cumming & Cumming, 1957). Psychotics were held in lower esteem than neurotics. There was a much narrower range of attitudes than of knowledge. More recent work has suggested that public attitudes may be favourably influenced by educational programmes (Peterson, 1986) or by direct personal contact with former patients (Trute & Loewen, 1978; Schwartz *et al*, 1974). The provision of services may have developed in advance of the public education necessary for these services to function effectively.

The needs of care-givers for support and information

The paramount need for consistent, carefully organised support is a recurrent theme in the literature on deinstitutionalisation (Mollica, 1983; Brown, 1985; Mechanic & Aiken, 1987). For the public, such support means education to deal with disproportionate fears. For patients' relatives, support translates into psycho-educational intervention, and counselling about the range of financial, vocational, domestic, and mutual-help services available (Falloon *et al*, 1985; Grunebaum, 1986; Creer & Wing, 1974; Marks *et al*, 1988). The employees and proprietors of public and private residential facilities in turn face the risk of isolation unless they receive professional consultation and statutory monitoring of their quality of care (Blaustein & Viek, 1987; Scull, 1985). The needs and views of staff during the transition from hospital must be dealt with directly (Bachrach, 1976; COHSE, 1984; Towell & McAusland, 1984) if misunderstanding and resistance are to be avoided (Talbott, 1978; Greenblatt & Budson, 1976). Finally, administrative support must be rendered to institutions in decline to maintain morale, adequate staffing levels and treatment standards, and to avoid staff 'burnout' (Mendal, 1979; Lamb, 1982).

Psychiatric services provided at the primary care level

General practitioners provide the overwhelming bulk of all care for psychiatric problems (Goldberg & Huxley, 1980), and about 8% of patients seen in primary care suffer from a chronic mental disorder (Wilkinson, 1988; Wilkinson *et al*, 1985). The redeployment of psychiatric staff outside the psychiatric hospital has generated new forms of collaboration between the primary and secondary care services. Over one-fifth of British psychiatrists now see patients in primary care centres (Strathdee & Williams, 1984). This may include a greater emphasis upon home visits, holding out-patient clinics in general practitioner surgeries, seeing selected patients at the request of family doctors, acting as a consultant to the primary care team, or seeing patients jointly with their general practice colleagues (Mitchell, 1985; Monk-Jorgensen, 1986).

The implications of transferring the locus of care from hospital

Homelessness and the failure of residential provision

Homelessness has rightly become a predominant issue in the North American literature concerning the chronic mentally ill (Bassuk & Gerson, 1978; Fischer & Breakey, 1986; Appelbaum, 1987; Farr, 1986). The National Coalition for the Homeless estimated that, in 1983, 2.5 million people were without accommodation in the USA (Bassuk, 1984). NIMH studies suggest that at least 30% of these suffer from serious and persistent mental illness (Morrisey & Levine, 1987). These recent surveys conducted in the period 1983–1986 in ten NIMH-funded centres were consistent in finding that the homeless mentally ill had multiple needs, tended to be long-term residents in their local areas, and had frequent police contact (Lamb, 1982).

Many of these 'new rootless' use emergency night shelters on a routine basis. Surveys at such shelters across the United States agree in indicating mental illness rates in the range 41–93%, alcohol dependency in over 60%, and chronic medical and dental problems in over 40% of this group (Bassuk *et al*, 1984; Fischer & Breakey, 1986; Kroll *et al*, 1986). These individuals characteristically had very restricted social support networks, little contact with psychiatric services, lower readmission rates than their domiciled counterparts, and little likelihood of referral to long-term care facilities (Appleby & Desai, 1985). Local psychiatric facilities clearly do not serve these homeless mentally ill at all adequately (Lamb, 1984).

The relatively scant British psychiatric research literature on the homeless mentally ill has focused on people living in lodging houses (Priest, 1976), reception centres (Leach & Wing, 1978), and those in prison or hospital who are of no fixed abode (Berry & Orwin, 1966; Herzberg, 1987). As in the North American studies, variations in the methods of case identification and the heterogeneity of the samples selected have produced a very wide range of values for the prevalence of such disorders. No clear findings have yet emerged. There is concern, however, from a series of small surveys of shelter users, that a large (36%) and rising proportion have a mental disorder, and that this may reflect the consequences of discharging psychiatric patients without adequate, or indeed any, follow-up (Weller *et al*, 1987).

What lessons emerge that may allow the prevention of homelessness among the chronic mentally ill? Drawing together the implications of this failure of public policy, the American Psychiatric Association Task Force on the Homeless Mentally Ill reported that homelessness was not a consequence of deinstitutionalisation *per se*, but of the way in which it had been carried out. It recommended the establishment of a wide range of local supervised housing options, and a greater provision of general medical care, peripatetic psychiatric services and crisis intervention, together with a secure and simplified source of income. It further recommended that the mental health services should become more integrated, based upon the case manager model, and that asylum should be provided for the small proportion of patients who continued to need sanctuary (Lamb & Talbott, 1986).

The integration of clinical responsibility

For psychiatric teams working with the chronic mentally ill, the concept of the 'case manager' is increasingly influential (Intagliata, 1982; Harris & Bergman, 1988). A particular staff member is given the primary responsibility for named patients. The case manager will act as advocate and as broker between the various service agencies concerned with each case, maintain the central therapeutic relationship, monitor the patient's well-being and progress, and plan social and occupational goals. The case manager model is increasingly used within the context of the multidisciplinary team (Mechanic, 1986) to ensure the maintenance of continuity of care, without which a high proportion of patients are lost to follow-up (Torrey, 1986; Bachrach, 1976; Tantam & Klerman, 1979). As yet, however, there is a paucity of evaluative research on the costs and effectiveness of case management (Franklin, 1988).

The administrative integration of services

The administrative integration of services has also been advocated within Britain through the allocation of development funds, competed for and administered by district-based Joint Mental Health Development Committees. In the National Health Service, current revenue expenditure on joint finance and per capita transfer payments amounts to about £100 million a year from a total expenditure of £3 billion for the mentally ill. The capital assets released by the closing of institutions may exceed £500 million (Audit Commission, 1986). The Griffiths Report (1988) proposed that local government social service departments accept responsibility for being the 'lead agency' in managing community services for the mentally ill, although the Department of Health is likely to recommend that District Health Authorities take on this 'lead agency' role.

There is a striking consensus in the literature on deinstitutionalisation that the variety of individual service components must be integrated into a programme of care (Stein & Test, 1980; Test & Stein, 1980; Mollica, 1983; Murphy, 1988). Such a programme should be based on clear public policy and priorities for the chronic mentally ill (Pepper, 1987; Murphy, 1987). Responsibility at each level needs to be clearly established. Measurable objectives for each element of the service must be defined and regularly reviewed, and this implies a regional or national inspectorate to monitor quality of care (Griffiths, 1988).

Financing deinstitutionalisation

How cost-effective are community-based forms of psychiatric care? In general, the more sophisticated the evaluation, the less apparent the cost advantage of home-based care. Weisbrod *et al* (1980) performed a cost–benefit analysis on an experimental home-based care programme in Madison, Wisconsin. They found additional annual costs for each person in the experimental group of $800, but this was outweighed by additional benefits totalling $1200, largely accruing from a doubling of patients' earnings. They were, however, unable to quantify 'hidden costs' (Bachrach, 1976; Scharfstein, 1978) such as the burdens upon neighbours, illegal activities, and the costs of occupation. Fenton *et al* (1982) compared home and hospital treatment for severely mentally ill patients. They found that manpower and operating charges formed the greater part of the total costs and were higher in the hospital group, but the group treated at home incurred greater costs for transport and medication. Although the relatives of the home-treated group had insignificant loss of work time, they commonly experienced symptons of depression.

A less complete evaluation of the range of costs incurred by a community care programme in Chicago demonstrated that a psychosocial programme could produce savings of between $2000 and $5000 annually for each patient (Bond, 1984). Using a randomised controlled design, Linn *et al* (1985) followed up 403 male chronic psychiatric patients allocated to community nursing homes, to hospital care and to two intermediate groups. Annual costs per patient in the nursing homes, at $20 000, was $11 000 less than for the hospitalised cases. The important point, however, is that the patients allocated to the nursing home showed significantly worse outcome in terms of self-care, behavioural deterioration, mental confusion, depression and satisfaction with care. A further randomised control design at the Quarterway House in Boston (Dickey *et al*, 1986), but using only 22 patients "who had no potential for community placement", compared traditional long-term hospital care with an experimental programme that provided an intermediate level of 24-hour care. There was no difference in clinical or social function at two-year follow-up but for the experimental group there was a total annual saving of $7000 per patient.

There is evidence that the transfer of patients from state hospitals in the USA has produced both a considerable cost saving and cost shifting. An analysis in the ten San Francisco Bay Area counties (Leavitt, 1984) estimated that this policy had produced a net annual saving of $400 million to each county and that when extrapolated to the State of California, this amounted to a saving of $1.3 billion, most of which had been diverted away from the chronic mentally ill. The introduction of Medicaid in the mid-1960s enabled both a transfer of obligation to be made from state to federal budgets (Mechanic, 1986) and a more rapid transfer of patients to nursing homes (Scull, 1985).

In sum, these studies tend to follow-up selected groups of patients over inadequate periods of time. They vary considerably in the completeness of estimating community-care costs. The more comprehensive community programmes tend to show less short-term cost saving and to require forms of bridging finance. Conversely, the least expensive successor services have been shown to offer an equivalent or worse standard of care than the asylum. The balance of current evidence is that adequate community care is no cheaper than inadequate hospital care.

Conclusion

How much progress has been made towards the British policy targets since the publication of the 1975 White Paper? The 67 000 remaining psychiatric in-patients in 1984 represented 45% of the total target reduction over the decade. The 6800 residential places were 41% of the proposed target increase, and the 17 000 day hospital places were only 17% of the target figure. The 9000 places available in day centres showed an increase of only 16% towards the stated target of 28 200. From these figures alone it is clear that the rate of hospital rundown has far outstripped the development of successor services (Audit Commission, 1986). On this evidence deinstitutionalisation is succeeding; new provision is not.

The dangers of deinstitutionalisation imperfectly implemented are clear. Those discharged face the prospect of isolated, segregated, impoverished, and under-stimulated lives. They have a high likelihood of homelessness and recurrent admission (Goldstein & Caton, 1983; Craig *et al*, 1984; Pepper *et al*, 1981; Bachrach, 1984*b*; Linn *et al*, 1985; Harris *et al*, 1986). In short, such discharged patients are at risk of multiple disadvantage and neglect (Bachrach, 1976). Seen in the longer historical perspective of cycles of care for the chronically mentally ill (Morrissey & Goldman, 1984), deinstitutionalisation has passed through a phase of the idealisation of community care (Banton *et al*, 1985; Minkoff, 1987). It may yet decay into the disillusionment of reinstitutionalisation (Elpers, 1987).

More positively, the following points emerge clearly from the literature. Community care, properly provided, can indeed improve the quality of life of the seriously mentally ill, but there will, however, be a continuing need to provide asylum for the most disabled patients. Adequate community provision is no cheaper than institutional care and will be more expensive in the bridging period, when elements of both services are provided. Finally, the full potential of community-based psychiatric services will only be realised where the administrative and financial structures exist to integrate local services into a co-ordinated programme of care.

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Lecture

Treatment of Depression
The Relevance of Research for Clinical Practice*

E. S. PAYKEL

My aim in this lecture is to review a wide range of published studies on the treatment of depression. I want to look at these with one major clinical question in mind: given the range of treatments available, which treatment should be chosen for which patient? In July 1985 a report, published as a special supplement to the *American Journal of Psychiatry*, called for more research on this topic:

> "As the number and diversity of the effective drugs and psychosocial interventions expand, clinicians will increasingly want objective, reliable criteria with which to match the patient to the optimal treatment modality and to monitor the response." (Institute of Medicine, 1985)

I wish to examine the extent to which this aim may already have been achieved. To establish some reasonably firm conclusions, I will also need to look to a lesser extent at the degree to which the treatments are effective.

I have chosen this topic for several reasons. The honour of an invitation to deliver the Maudsley Lecture encourages a certain internal deliberation about a suitable subject. Treatment is a central activity for the psychiatrist: it is the main reason why the world wants his existence. However, this is not the occasion for a straightforward practicum of treatment. As a research topic, much of my own work over 25 years has been concerned with prediction of response and indications for therapeutic choice in depression.

As a second major theme, I want to illustrate the place of research in relation to clinical practice. I will synthesise many studies to draw conclusions about specific treatments. In doing so I will try to illustrate the value of treatment trials, and, particularly, to explore the two-way process by which clinical insight informs the genesis of good studies, and in turn sound methodological investigations are essential for firm conclusions about clinical treatments.

Causative models and therapeutic modalities

Treatment of depression also allows one to illustrate a fundamental principle in psychiatry: the value of multiple approaches. Akiskal & McKinney (1975), in a review, described ten partially overlapping models of depression, ranging from impaired monoaminergic neurotransmission to loss of the meaning of existence. They covered five broad areas – psychoanalytic, behavioural, sociological, existential and biological. These explanatory models need not be regarded as antithetical, but all may converge on a final common pathway. All the evidence indicates that causation of depression is multifactorial. No single factor is of overwhelming importance, except possibly in bipolar disorder, where there may be single genes of major effect. Otherwise depression has many causes, with an amalgam of genetic make-up, early environment, physical factors and recent social stresses. One should not make an artificial dualistic separation between the biological and the psychological, since psychosocial stresses are mediated via the brain.

In a disorder of complex aetiology it would seem unlikely that a single form of therapy would serve all cases. The social, the biological, the psychological, are as valid as approaches for treatment as for causation, and for theoretical models. The eclectic therapist will assign importance to all three modalities, and he or she will be careful not to infer a particular cause from a particular therapeutic response. For drugs and for psychological approaches I will show detailed evidence, since there have been many studies. As a social psychiatrist I would like to be able to deal equally thoroughly with social aspects of treatment, such as family support, rehabilitation and environmental manipulation. Unfortunately these have been less subject to controlled evaluation. Probably one of the most powerful treatments for severe depression is admission to hospital: many clinicians and biological depression researchers will have had the experience of watching a psychotically depressed patient improve markedly after admission to a supportive ward milieu, while drug treatments or electroconvulsive therapy (ECT) are being withheld. Equally, for mild depression there are probably major supportive effects from out-patient assessment by a psychiatrist, with the unusual experience of spending up to an hour reviewing in detail one's recent problems and life-history to a sympathetic listener.

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*Maudsley Lecture, delivered to the Royal College of Psychiatrists on 26 October 1988.

Methodological requirements

We need also to consider the methodological requirements for conclusive studies. The essential test for efficacy and for specificity is the controlled trial. Many studies in the past have adopted a single group predictive design. One takes a mixture of depressed patients, treats them for six weeks with a single antidepressant, rates them at beginning and end of treatment, and then examines by some statistical technique to see what characteristics at the beginning distinguish those who have done well and badly on the treatment. Although such studies may drop useful hints, this design is not enough.

In any patient who improves or recovers on treatment with an antidepressant, a number of different elements may contribute to the response. First, it may have been spontaneous, reflecting the natural history of the disorder. Spontaneous remission is probably not uncommon. It is clear from historical accounts that severe melancholia in the nineteenth century did in due course remit: the recognition of this remission contributed to Kraepelin's delineation of manic depressive disorder by its course. Modern high prevalence and episode rates for mild depression in the community make it clear that much of this disorder remits without ever being recognised or treated.

Secondly, many other treatment processes are also at work in a patient who receives an antidepressant, such as the social effects of ventilation, support, and hospital admission already referred to, and the effect of receiving an inert placebo. The placebo group in drug trials controls for everything except the specific effects of the chosen antidepressant treatment. The limited evidence available (Paykel *et al*, 1975) suggests that the effects of the placebo itself are in fact quite weak, but the effects of other non-specific treatment factors are probably quite powerful. The specific effects of the drugs are not very large. In placebo-controlled trials in depression, as a rule only 20–30% more recoveries occur on active treatment than on placebo.

When predictor analyses of response only examine the change in a group of subjects given the single treatment under investigation, improvement is an amalgam of the above factors, and it is not possible to say to which element significant predictors are related. If one wants to say that a certain treatment is indicated for a specific patient, one needs to focus on the specific effect of the treatment, i.e. the magnitude of the difference between improvement on this drug and on placebo or alternative treatment. One needs to show that this difference is greater in the patient group under consideration than it is for other treatments which might be given instead. This requires a controlled trial against placebo or an alternative treatment. Probably the best technique is the factorial design with two-way analysis of variance of treatments by classification subgroups where one seeks a significant interaction term indicating that differences between the two treatments are of different magnitude in different patient groups (Paykel, 1988).

I will now look for this kind of efficacy and any groups specifically responsive to five classes of treatment: ECT, monoamine oxidase (MAO) inhibitors, tricyclic antidepressants, dynamic psychotherapy, and cognitive therapy.

Electroconvulsive therapy

ECT is the oldest of the current antidepressant treatments. It illustrates one earlier pathway between clinical care and research – clinical innovation, in which research designs followed much later. The clinical innovation followed a mistaken and accidental road that seems almost classical for new treatments in psychiatry. Von Meduna's use of chemical convulsions was based on the belief that epilepsy protected against schizophrenia; the truth, at least for temporal lobe epilepsy, turns out to be the reverse. He, and Cerletti and Bini, used convulsive therapy for the wrong disorder: its most useful place is in depression.

It is easy to feel that if dramatically effective treatments came along in psychiatry, controlled trials would no longer be necessary, and of course they played no part in the introduction of ECT. It is therefore interesting that in the long run they became necessary, in response to public questioning of the value of the treatment.

Among the most remarkable of studies have been the six recent blind comparisons of ECT and simulated ECT carried out in Britain. The first of the studies (Lambourn & Gill, 1978) showed virtually no benefits and the Northwick Park study (Johnstone *et al*, 1980*a*) found effects that were less strong than might have been expected, but the remaining studies showed strong treatment effects among groups of relatively severely ill in-patients (Freeman *et al*, 1978; West, 1981; Brandon *et al*, 1984; Gregory *et al*, 1985).

It is instructive to ask why the studies differed in their findings. One possibility is that the negative study was the only one to use ECT applications that were unilateral and brief pulse. There is some evidence that sine wave applications are more effective than brief pulse, at least when delivered at low energy (Robin & de Tissera, 1982), and more clearcut evidence that bilateral ECT is more effective than unilateral (D'Elia & Raotma, 1975; Abrams & Fink, 1984; Sackeim *et al*, 1987), probably because induction of convulsions is more reliable.

ECT was the target of the earliest predictor studies of specific antidepressant treatments. Hobson (1953) constructed a predictor index in which the items were very similar to those distinguishing psychotic and neurotic depressives, although he did not adopt that terminology. Since then, a moderately large number of studies have concluded that psychotic depressives show better response (Paykel, 1979), the main dissenting study being that of Abrams *et al* (1973). All these studies were without control groups and did not conform to the design I have advocated. One study which did do so was the Massachusetts collaborative study (Greenblatt *et al*, 1964). In this controlled trial, non-blind with respect to ECT, breakdown by diagnosis showed, among manic depressive illnesses (bipolar and unipolar in modern terminology), 78% markedly improved on ECT as opposed to 37% on placebo; among involutional psychoses 85% against 25%; for psychoneurotic depressive reactions, 77% against 83%. In addition, the Northwick Park study (Clinical Research Centre, 1984) in subsequent analyses found that the superiority of active ECT was mainly in patients with depressive delusions.

Published studies of ECT almost exclusively involve in-patients in the severely ill range. Among such patients, ECT does appear to be more effective than tricyclic antidepressants and MAO inhibitors. There have in fact been a number of non-blind randomised comparative trials with random assignment (Paykel, 1979). Among nine comparisons with tricyclic antidepressants, six found ECT better overall, while three studies found equal drug effects. Among comparisons with MAO inhibitors, the superiority is even more striking, with ECT more effective in all five studies (Greenblatt *et al*, 1964; Medical Research Council, 1965; Kiloh *et al*, 1960; Hutchinson & Smedberg, 1963; Stanley & Fleming, 1962). No study has found drug treatment more effective overall than ECT. This shows a pattern which is frequently found in surveying therapeutic trials in psychiatry: two treatments are found equal or treatment A is found better than treatment B, but rarely or never is B better than A. What this usually indicates is some, although limited, superiority of A over B: it shows up in some situations with some samples but not in others.

Monoamine oxidase (MAO) inhibitors

With the MAO inhibitors the link between clinical practice and research was different: a story of drugs introduced just before the beginning of the era of controlled trials in psychiatry, and of the insight of a charismatic clinician as to their specific place slowly being subjected to controlled testing by others with some confirmation. The clinician who first crystallised a view of the selective clinical place of MAO inhibitors was William Sargant. His ideas first clearly emerged in a paper by West & Dally (1959), who described a syndrome of atypical depression. There have been many subsequent papers.

Three different meanings have really been assigned by different authors to the term atypical depression (Paykel *et al*, 1983). One is the idea of marked anxiety and phobic symptoms, either accompanied by depression, or assumed to have some relation to an underlying depression as indicated, for instance, by diurnal variation. This has included the influential views of Tyrer (1976).

The second meaning is what Pollitt (1965) describes as reversed functional shift, i.e. depression with a diurnal pattern of evening worsening, insomnia of early rather than late kind or increased sleep, increased appetite and weight, all in the direction opposite to the physiological changes said to characterise endogenous depression. In the USA Donald Klein, another charismatic clinician, who conducts controlled trials to test his insights (Liebowitz *et al*, 1988), assigns principal importance to these features.

A third meaning of atypical depression, at one time common in the American Literature (Robinson *et al*, 1974), was that of non-endogenous depression in general. This usage has gradually dropped out in the last ten years.

These three meanings identify different groups of patients. In a sample of out-patient depressives we collected a large amount of diagnostic data on many different subclassificatory systems (Paykel *et al*, 1983). We examined the relationships between different diagnostic systems, using separate criteria for the three aspects of atypical depression. The three separate criteria tended to select quite different patients. We had to conclude that the concept of atypical depression was imprecise. It would be better to specify which aspect was to be emphasised.

The best evidence on the efficacy of MAO inhibitors is for phenelzine. Among seventeen controlled trials against placebo in depression (Paykel, 1989) ten have shown the drug to be clearly superior to placebo, three have been doubtfully positive, and four failed to show drug superior to placebo. For isocarboxazid, three trials have shown superiority over placebo and three have failed to. For tranylcypromine, two studies have been positive, one equivocal, and one negative (Paykel, 1989). This is less impressive than for ECT or for tricyclic antidepressants. There are also a number of positive studies in phobic disorders.

In these studies there was not a very strong relationship between response and defined subtype, but there was a clear relationship to treatment setting. All except one of the studies showing drug–placebo differences have been in out-patient samples; all the negative studies have been carried out on in-patients. Studies in day patients or mixed patients have tended to be equivocal. The most likely explanation would be that this reflects diagnostic subtype, since out-patients tend to be less severely ill and more neurotic in symptom pattern. Some re-evaluation may be needed here since most of the in-patient trials were early studies, using doses and treatment periods that were relatively low by modern standards.

We conducted a controlled trial of phenelzine, amitriptyline and placebo in out-patient depressives and mixed anxiety depressives. Overall we found clear drug effects for both drugs, with surprisingly little difference between them. On depression measures amitriptyline was minimally superior to phenelzine and on anxiety measures phenelzine was minimally superior to amitriptyline. These differences between the drugs, although in the predicted direction, were weak (Rowan *et al*, 1982).

We also undertook a series of two-way analyses of covariance with the various kinds of atypical depression as the second factor in the design (Paykel *et al*, 1982). Subclassifications based on presence or absence of additional anxiety symptoms gave some interactions, although they were not very strong. Phenelzine tended to be superior to placebo in those depressives with an admixture of anxiety but not in those depressives without anxiety. However, amitriptyline was effective in both groups. Neither of the other two views of atypical depression gave significant interactions with drug response.

Overall the findings of this study suggested some selectivity of MAO inhibitors in patients showing anxiety, but the difference was weak. In this mildly ill, neurotic and somewhat anxious group of depressives, usually not regarded as showing much benefit from tricyclic antidepressants, amitriptyline was clearly superior to placebo, and did not show any particular selectivity.

These weak differences between tricyclics and MAO inhibitors are consistent with other recent studies. Ravaris *et al* (1980) found only weak differences between amitriptyline and phenelzine, with phenelzine having more effect on anxiety measures. Davidson *et al* (1986), analysing patients from a number of studies, found weak trends for better effects of MAO inhibitor rather than tricyclic where a precipitant was present and, contrary to expectation, in the absence of agoraphobia. There were also some inconsistent predictors in the two sexes.

Liebowitz, Klein, Quitkin and colleagues have found stronger differences (Liebowitz *et al*, 1988). Selecting patients with reversed functional shift, they found phenelzine most effective; imipramine was less so, although better than placebo. Examining subgroups within this selected sample, they unexpectedly found that superiority of both phenelzine and imipramine to placebo was largely confined to patients with spontaneous panic attacks and/or hysteroid dysphoric features. Davidson *et al* (1988), in a comparative trial of isocarboxazid and placebo, found the drug more effective in endogenous depressives but also in patients with reversed functional shift, in anxious and in hostile depressives. In general these studies suggest some convergence of anxiety and reversed functional shift, but still the overall impression is of weak differences.

Taken overall then, a general conclusion for MAO inhibitors would be that they are weakly selective for anxiety and reversed functional shift, but the differences from tricyclics are not sufficiently strong to guide treatment choice consistently. Since tricyclics are safer and easier to use, the logical place for MAO inhibitors is as a second choice where tricyclics have failed and ECT is not indicated.

It remains possible that there is some other variable, rather than clinical symptom subtype, which predicts a better response to MAO inhibitors. Most clinicians are used to having some patients under their care who seem to respond only to this class of drug, and previous good response is probably the best indication for use as first choice. Supporting this view, Pare & Mack (1971), comparing outcome in patients who in successive episodes had received antidepressants of the same type or of different type, found a significant tendency for consistent response in the same direction, i.e. good or bad, with the same class of drug, and inconsistent responses across different kinds of drug. They also found some consistency in responses among relatives. This was a small study which needs repeating, but it does support the view that there are some specific response factors which might be related to biochemical variables only weakly reflected in symptom pattern.

Tricyclic antidepressants

Tricyclic antidepressants lie squarely in the controlled trial era. Discovery was rapidly followed by a model placebo-controlled trial carried out in Britain

(Ball & Kiloh, 1959). From the point of view of efficacy, they are well-evaluated drugs. A useful review was published by Morris & Beck (1974). Surveying the limited selection of tricyclic antidepressants then available in the USA, they found 93 comparative trials against placebo. This gives some idea of the relentless effort that goes into drug evaluation nowadays. Among these, 61 showed drug superior to placebo and 32 failed to do so. There will be more positive studies of additional drugs by now, so the evidence for efficacy is impressive. Some of the negative studies can be attributed to poor trial technique, such as short treatment periods, low doses and unsatisfactory outcome measures. Some undoubtedly reflect the limited benefit obtained from these drugs.

The view that tricyclics are particularly effective in endogenous depression has an impressive lineage, going back as early as the intitial open studies by Kuhn, and the first controlled trial. However, a critical look at the controlled trials published in the 1960s suggests that, although the effect may have been a little better in endogenous depressives, there was evidence of benefit in neurotic depressives (Paykel, 1979). Certainly there have been many trials, in which a tricyclic was superior to placebo in samples characterised as neurotic or reactive (Ball & Kiloh, 1959; Wittenborn *et al*, 1962; Uhlenhuth & Park, 1964; Covi *et al*, 1974; Friedman, 1975; Paykel *et al*, 1982).

The more recent literature regarding delusional depression also suggests a poor response to tricyclics and better to ECT or neuroleptics (Perry *et al*, 1982). It would appear that the most severe endogenous or psychotic depressives do not respond very well to tricyclics. There may be a curvilinear relationship in which the best response is shown by patients with the endogenous symptom pattern but moderate severity. This was found in two studies by Coppen and colleagues, using the Newcastle Scale (Rao & Coppen, 1978; Abou-Saleh & Coppen, 1983).

There is increasing evidence that tricyclics are superior to placebo when neurotic states other than depression are present. Marks (1983) reviewed a number of studies showing tricyclics to be superior to placebo when obsessional neurosis or agoraphobia were present. The obsessional studies depend mainly on one drug, clomipramine, with a more serotoninergic action, but the studies in agoraphobia have employed more standard drugs. Two important studies including a spectrum of anxious and depressed patients have not received the attention they deserve. Johnstone *et al* (1980*b*) treated such patients with amitriptyline, diazepam or placebo. Amitriptyline was consistently superior to placebo while diazepam showed only weak effects, even in patients with predominant anxiety. Kahn *et al* (1986) carried out a similar study with imipramine, chlordiazepoxide or placebo, with similar findings.

We examined effects of tricyclics in mild depression by means of a controlled trial in general practice. Depressives identified in general practice were treated for six weeks with amitriptyline or placebo double blind (Paykel *et al*, 1988; Hollyman *et al*, 1988). Mean initial total scores on the 17-item Hamilton Rating Scale for Depression were a little below 15, confirming the relative mildness of the sample. Differences started to appear surprisingly early and at two weeks had reached significance. By six weeks highly significant differences had appeared on a wide variety of typical depressive symptoms, with amitriptyline impressively superior to placebo.

To examine for responsive subgroups we carried out a series of two-way analyses of covariance, using as the second factor a variety of classifications from the literature. Significant interactions were relatively few, indicating fairly strong and consistent drug effects across most subgroups. Subgroups failing to give rise to interactions included demographic variables, history of chronicity, and endogenous versus neurotic depression.

Only in one area, severity, were there interactions. Active drug was beneficial to Research Diagnostic Criteria major depressives, with clear superiority over placebo. Minor depressives improved equally on drug and placebo. On initial Hamilton score we divided the sample into three groups: the most mild, with Hamilton scores below 13, those intermediate, with initial scores 13 to 15 and the relatively more severe, comparable with psychiatric out-patients. It was only the very mildly ill patients who showed no benefit from active drug: there were considerable drug–placebo differences for the two other patient groups, and again the effect was to produce final scores from amitriptyline close to those of the mildly ill.

These findings are consistent with another study in the literature. Stewart *et al* (1985) found desipramine to be superior to placebo when major depression was present, both with and without melancholia, but not dysthymic disorder. It was also effective in patients with initial Hamilton scores of 14 to 18 but not in those with scores of 13 and under (Stewart *et al*, 1983).

The real conclusion about tricyclic antidepressants appears to be that they are truly broad spectrum antidepressants, effective across quite a wide range of depressions, extending to clearly non-endogenous and relatively mild disorders, although with a floor level for severity, and also well into the spectrum of anxiety disorders. They make a good first choice where medication is to be used: the indication is the presence of an established depressive syndrome of all but very mild severity.

Psychotherapy

With the dynamic psychotherapies we extend into another area of clinical-research interrelationship: that of the fierce and dogmatic therapeutic debate where research, rather surprisingly, acts as the peacemaker. Historically drugs and psychotherapies have often been diametrically opposed, with proponents of each arguing that the other was at best limited and at worst harmful. Each was opposed to combined therapy, drug therapists arguing that psychotherapy merely stirred up feelings that made the patients feel worse: psychotherapists that drugs fixated the patients on symptom and somatic issues.

The controlled studies have all come out of the USA and it is interesting that the earlier ones were funded by the Psychopharmacology Research Branch, that part of NIMH which supported drug trials. They were really successful transplants of the methodology of drug trials to psychotherapy.

The first Yale–Boston collaborative study (Paykel *et al*, 1976) was a continuation study of amitriptyline versus withdrawal in depressed women, half of whom were assigned to receive once weekly individual psychotherapy from social workers and the other half once monthly low contact. Psychotherapy did not lower the relapse rate but had a clear effect in improving social adjustment and interpersonal relationships. Psychotherapy was only effective after eight months' treatment, and only in patients who had not dropped out because of earlier relapse, so that the best benefits were from the combination.

Using acute treatment with amitriptyline or placebo with and without conjoint marital therapy, Friedman (1975) found that marital therapy improved marital relationships with a little benefit on symptoms also; amitriptyline had much more effect on symptoms. Again, combination was best. In a third study Covi *et al* (1974) found little effect from group therapy, but this study lacked social adjustment measures and there were hints of effects on the limited measures which were incorporated.

A further study from Yale and Boston used amitriptyline, individual psychotherapy from psychiatrists, both treatments, or no treatment and found a different pattern (DiMascio *et al*, 1979). Drugs and psychotherapy both had effects in improving symptoms. The combination produced the most improvement.

These studies all suggested that psychotherapy was of value, but in the first three it was primarily for interpersonal relationships and social maladjustment and drugs were more effective for the symptoms of depression. The split between symptoms and social effectiveness was exactly what had been suggested many years before by Jerome Frank and his colleagues (Parloff *et al*, 1954). All found that drugs and psychotherapy worked well in combination to produce the maximum benefit.

The most recent study is the large collaborative study in which depressed out-patients were randomly assigned to receive imipramine, interpersonal psychotherapy of the kind used in the Yale–Boston studies, cognitive therapy, or placebo (Elkin *et al*, 1985). This was an expensive study and great care was taken over training. Some results have been reported at meetings, but not yet published. Overall, the three active measures produced benefit compared with placebo, although cognitive therapy was a little the weaker of the three. The benefit was on the same symptom measures. This study gives food for considerable thought. It suggests that drug, a dynamic psychotherapy and a cognitive behavioural one, can all produce similar improvement in symptoms. Perhaps a pathway can be altered at various points along the way to produce a final common consequence.

Most of these studies did not report analyses directed towards the question of who responds best to which therapy. All were conducted in out-patients and they do not permit conclusions regarding severely ill in-patients. The second Yale–Boston study did analyse by Research Diagnostic Criteria subtypes of major depression. Amitriptyline showed the best effects in RDC endogenous depressives: psychotherapy in situational depressions (Prusoff *et al*, 1980). Endogenous depression is defined in the RDC in terms of symptom pattern, situational depression in terms of social stress, so the two are not mutually exclusive. Analyses of the NIMH collaborative study reported so far do not show clear selectivity for interpersonal psychotherapy.

Probably the best guidelines at the moment are that psychotherapy is appropriate for tackling psychodynamic and interpersonal problems when these are present. It is best combined with antidepressants: it may produce some symptoms remission, at least in the milder patients. Combination with drug therapies is highly desirable. Clinically it is often unproductive to use psychotherapy in the more severely ill until symptom remission due to drugs or ECT makes it possible.

Cognitive therapy

Cognitive therapy is the Yuppie of the antidepressant therapies: a child of the 1970s, verbal, exciting, a little pushy, perhaps riding for a fall. Again, its introduction has depended on a charismatic clinician, Aaron Beck. Controlled evaluation appeared early in its history, reflecting a birth well within the controlled trial era. A recent review (Dobson, 1989) identified 21 controlled trials, but not all were very informative in design. Studies in clinically depressed samples (out-patient or general practice) are particularly useful. Five studies, including the NIMH collaborative study, have made comparisons with drug (Rush *et al*, 1977; McLean & Hakstian, 1979; Blackburn *et al*, 1981; Murphy *et al*, 1984). All found the two approximately equally effective on symptom measures: sometimes cognitive therapy was a little more effective than drug: sometimes, as in the NIMH collaborative study, a little less. A sixth study (Teasdale *et al*, 1984) found it as effective as GPs' routine treatment. A recent study (Beck *et al*, 1985) found cognitive therapy plus drug no better than cognitive therapy alone.

Again, samples were out-patients with mild to moderate rather than severe illnesses, so conclusions must be limited to such patients. Most of the studies have had too small samples to look for responsive subgroups. In the NIMH collaborative study analyses reported so far, benefit from cognitive therapy was mainly in the more mildly ill among the patients studied, with drug and interpersonal therapy more effective in the moderately ill.

The ultimate place of cognitive therapy is not yet clear. Cognitive therapists with whom I have discussed it tend to feel that it is not useful in chronic, and resistant cases, and that the sort of patients who do well are also those who respond well to drugs. In this case its place would be limited to those who are reluctant to take antidepressants: cognitive therapy involves a lengthy treatment process for up to 16 weeks: drug therapy is cheaper and less intrusive, with much less investment of patient and therapist time. It is quite likely that briefer or even largely self-help methods of cognitive therapy will be developed.

There is an intriguing further finding: some evidence that cognitive therapy may cut down the rate of relapse, which can be quite high after drug therapy. Three studies which compared tricyclic antidepressant with cognitive therapy in initial treatment have found on follow-up for 6–24 months that relapse rates were much lower in the cognitive therapy group than in those who received tricyclic antidepressant (Hollon *et al*, 1984; Simons *et al*, 1986; Blackburn *et al*, 1986). The differences were substantial, from 66%–78% on drug to 12%–25% on cognitive therapy. Each study included a group receiving combined therapy, and in two of the three studies (Hollon *et al*, 1984; Blackburn *et al*, 1986) they also had low relapse rates. Two other follow-ups (Kovacs *et al*, 1981; Beck *et al*, 1985) have failed to find this benefit for relapse rates.

These findings require replication and extension. Samples of patients in naturalistic follow-ups may not be comparable: different patients may respond to drugs and to cognitive therapy. Drug continuation would make a better comparison than the relatively early drug withdrawal that has occurred in some of the studies. If the findings are sustained, cognitive therapy will have a major place in those depressives prone to relapse.

Conclusions: research and clinical practice

I have tried to summarise many efficacy studies all directed, at least in part, to the question of which specific treatment is indicated for which kind of patient. One of the tasks which I set myself was to see if the aspiration of matching patient and treatment choice had already been achieved. The answer is "yes, to some extent". The broad outlines of who responds best to which treatment are already clear, and tend to confirm long-held beliefs, but there is much variation between individuals and when one applies the criteria for choice to the single patient, there is not high predictability, particularly for the more resistant patients. We are left with some guidelines for first choice and for combining drug and psychological treatments, but the recognition that not uncommonly a less obvious second choice is necessary.

A more general implicit conclusion is that modern treatments are effective. Prior to the introduction of ECT, although the old accounts indicate that patients did improve and recover, the spontaneous course might be quite a long one, and in-patient acute wards were fairly accustomed to the long stay in hospital of persisting psychotic depressives. Nowadays, even if we do need better treatments, even if chronicity does occur and relapse is often a problem, the majority of depressives show considerable improvement within a few weeks or, at the most, months of starting treatment. Severe resistant depression is the exception.

One of my aims has been to illustrate the relationship of therapeutic research and clinical practice. One theme which clearly emerges is the change over the years in the processes by which new treatments become established. In earlier times in psychiatry, and presumably for many centuries in the history of medicine, the process was one of individual treatment innovation. Innovators were striking, often charismatic, personalities. Dramatic effects were expected but rigorous proof not demanded nor the requirement for its demonstration appreciated. Within depression, ECT and the older dynamic psychotherapies followed this path. The introduction of the earlier drug treatments showed some similarities with this process but it was rapidly overtaken by the need for controlled trials.

There is a remarkable contrast between the earlier innovations and the careful, measured, and perhaps rather plodding evaluation which precedes the introduction of a new antidepressant today, with all its formal panoply of governmental regulatory oversight. A historian might pay special attention to the place of cognitive therapy, introduced by a charismatic innovator, free of the somewhat limiting constraints which would have accompanied the development of a new drug, yet evaluated by controlled trials from the beginning, because of the scientific climate of the time.

Controlled trials have a special place in what I have said. There have been various criticisms over the years of this methodology. Surely it is rather dull? Is it ethical? Is it misleading because of selection factors? Is it unnecessary because there are other ways of seeing if a treatment works, such as comparisons with experience before the introduction of the new therapy? A good trial has several elements, including random assignment, double blindness, sensitive assessment measures, appropriate data analyses. Among these it is the random assignment to groups treated at the same time with different treatments which is most crucial. The contribution of controlled trials in producing clear-cut answers for the therapist has been extremely high and it remains essential. Outcome measures are too unreliable, effects of bias and expectation too strong, and effects of treatments on the whole too weak in psychiatry, to do without them. Trials are sometimes belittled by researchers as dull and unimaginative. I would rather praise this essential work.

With respect to the specific treatments, the conclusions of this review of a relatively large number of studies, although they have challenged in one or two places earlier cherished beliefs, have tended to confirm modern clinical practice. If, like Molière's *Bourgeois Gentilhomme*, we have discovered that we have always spoken prose, that is not surprising, because the pathway between research and clinical practice is a two-way street. Research confirms clinical practice because clinical practice has been modified by research, and research questions shaped by clinical practice. A very large volume of research has gone into the generation of even tentative conclusions about the place of specific treatments. In treatment studies no single study can be relied on as a definitive example of the revealed truth: findings vary from study to study, depending on the detailed variations in treatments, patients, assessment and analyses. Taken together the studies do in the long run make a consistent picture.

My concluding point must be to highlight the interdependence of research and clinical practice. Therapeutic research can only be relevant when it is anchored in the major questions of clinical practice. Clinical care depends for its advance, and for its validation, on a foundation of painstaking therapeutic research.

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The History of General Hospital Psychiatry

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General hospital psychiatry in Britain began in 1728, and thereafter several new voluntary hospitals provided separate wards for lunatics, but none survived beyond the middle of the 19th century. Less severe nervous organic disorder has always been common in the general wards of voluntary hospitals, and was accepted as the responsibility of neurologists and other physicians; all forms of disorder were admitted to the infirmaries of workhouses. During the present century psychiatrists began to take an interest in non-certifiable mental illnesses and in working in general hospitals. Out-patient clinics became more common following the Mental Treatment Act 1930. The growth of general hospital psychiatric units in the last 30 years began amidst controversy, but has received little recent critical attention.

General hospital units, which now care for 40% of all new psychiatric admissions in England and Wales, are usually seen as a recent innovation, but in fact (Allderidge, 1979) there is a long history of the care of psychiatric disorder in general hospitals. During a short period in the later 18th and early 19th centuries, several general hospital psychiatric wards were opened for reasons similar to those advanced today.

This review considers two main themes: the first is the history of the treatment of major mental illness (lunacy, insanity) within general hospitals; and the second is the management within medicine, surgery, and neurology of emotional disorders and functional somatic symptoms, which have only recently been seen as a part of psychiatry.

Voluntary general hospitals in the 18th and 19th centuries

In the medieval period, mentally ill people were not uncommonly treated in hospitals and religious institutions (Porter, 1987). The first hospital as we know it in England was St Bartholomew's, established in 1123 to provide for the needy, poor, and sick of every kind. Few of these institutions survived the Reformation, however, and at the beginning of the 18th century there were only two general hospitals in London – St Thomas's and St Bartholomew's. During that century, though, social changes and the philanthropic movement resulted in the foundation of new hospitals. The first general hospital to admit lunatics was Guy's. Thomas Guy obtained land from St Thomas's, of which he was a governor, and left money in his will for a hospital for incurable patients, directing that it should "receive and entertain lunaticks, adjudged or called . . . incurable, not exceeding twenty at one time". Guy's Hospital opened its separate 'lunatic house' in 1728 (Hunter & MacAlpine, 1963). A few years later, in 1736, the French Protestant Hospital in London added places for 42 patients, mainly elderly, who had suffered mental distress due to torture or privation before leaving France.

Other new voluntary hospitals were not endowed by benefactors, but depended on regular subscriptions from wealthy people or institutions, who were rewarded with the right to nominate those deserving of admission. The Westminster Hospital (1720) was the first; 13 more subscription hospitals opened during the century in London, 28 in the provinces, and five in Scotland (Woodward, 1974; Busfield, 1986).

Some voluntary general hospitals included accommodation for the insane. The Edinburgh Royal Infirmary (1741) had a ward of 12 vaulted cells on the ground floor (Risse, 1986): admissions came from all social classes, but upper-class patients were preferred because they could pay for their own care and brought their own servants. Manchester opened its lunatic hospital in 1766 as an annexe to the Infirmary, as did Liverpool, in 1749, and Leicester, in 1794.

However, none of the voluntary-hospital lunatic wards survived beyond the mid-19th century. In Edinburgh, it was recorded as early as 1795 that "the managers of the Royal Infirmary have for many years past declined the admission of such persons" (Risse, 1986). In contrast, the Manchester Lunatic House had more than 100 beds in 1800, but by 1844/45 it was half empty, apparently because of the competition from private care and the new pauper asylums. Attempts by the hospital staff to close it and appropriate its endowment for the main infirmary were declared illegal and instead it moved to become the Cheadle Royal Hospital (Jones, 1972; Pickstone, 1985).

Guy's Hospital continued to care for incurable lunatics until 1859, although admissions had been restricted since 1805, and the poor facilities and lack of medical care were repeatedly criticised by the Commissioners in Lunacy (Munro, 1954).

Most voluntary hospitals specifically excluded lunatics from their foundation. The rules of the Radcliffe Infirmary, Oxford, from 1770, stated that "no persons disordered in their senses . . . be admitted as patients; or if inadvertently admitted, be not suffered to continue". Inevitably, though, some lunatics were "inadvertently admitted", as a complaint in the 1839 General Visitors Book shows:

> "Charlotte Fraser, the lunatic who was surreptitiously sent into the infirmary in consequence of having a broken thigh, continues to occupy the whole of the fever ward to the exclusion of any other patient and to require the entire services of Nurse Gillard, and occasionally of others. The attention of the weekly board is requested to this case. It appears no very legitimate use of the charities of this house to introduce a patient, known to be a lunatic without stating the fact to the officers."

Inevitably also, some patients with physical problems developed certifiable mental illness during their admissions. The records of the Radcliffe Infirmary contain repeated references to such problems. For example, on 6 January 1886, "the house surgeon reported that John Lockton of Elsfield, a patient in Frewin Ward had committed suicide early this morning". Most insane patients were rapidly discharged, although occasionally they were transferred to asylums. In 1859, it was recorded in the Minute Book of the Radcliffe Infirmary that "Ambrose Eeles, an in-patient, being of unsound mind and from his behaviour improper to remain as a patient, the Chairman was required to write to his parish to remove him". Three weeks later, the Minute Book notes that a complaint was received from the clerk of the visitors of the county asylum at Littlemore, expressing surprise at the discharge of the patient from the Radcliffe, and stating that "he has shown no symptoms of lunacy since he has been in the asylum". Even so, "it was resolved after a careful examination that Ambrose Eeles was properly discharged, being of unsound mind and able to be removed with perfect safety".

Some forms of what we would now see as psychiatric disorder were always accepted in the general hospital, for example less severe non-certifiable disorders and odd behaviour and delirium as complications of physical illness and childbirth (Marland, 1987; Rushton, 1988). Records show an even wider range of psychological disorder in out-patient clinics (Marland, 1987). It was sometimes difficult to decide who should be excluded, though, and when the Radcliffe Infirmary house physician asked for advice, he was told that out-patients "of doubtful sanity" should be admitted temporarily until seen by the physician of the week.

Behavioural and emotional disorders

Many admissions for hysteria, hypochondriasis, and apparently functional somatic symptoms are recorded in surviving 18th-century and 19th-century admission and discharge books, such as those of the Edinburgh Royal Infirmary (Risse, 1986, 1988). For instance, the Radcliffe Infirmary book for 1812 lists five of the 572 in-patients and eight of the 253 out-patients as "nervous", with two out-patients suffering from hysteria. Many others were diagnosed as suffering from debility, pain, palpitations, dyspepsia, and other symptoms which may have had a psychological cause.

The disorders of the nervous patient, which included hypochondriasis (Fischer-Homberger, 1979) and neurasthenia, were seen as having an unknown but undoubtedly organic aetiology. Until well into the 20th century, these problems were the responsibility of physicians, and of the developing specialty of neurology (Bynum, 1985). Thus, neurologists at the National Hospital, London, routinely recorded the mental state of their patients (Hunter & Hurwitz, 1981). In contrast, specialists in mental illness who worked in private madhouses and in the asylums concerned themselves largely with certifiable lunacy or insanity, and took only a limited interest in other psychiatric disorders.

Organic disorder and other psychological problems

Delirium complicating serious physical illness, such as puerperal and other fevers, was always accepted as a responsibility of general hospitals; the case notes at the Edinburgh Royal Infirmary give many details (Risse, 1986). Some hospitals had private rooms or special areas for disturbed patients (Thompson & Goldin, 1975). For instance, Guy's had a 'strong room' on the top floor, where patients were tended by porters rather than nurses (Munro, 1954). The Liverpool Royal Infirmary had a small ward, called the DT No. 10, for acute cases – "many of them alcoholic, others not so" (see Clouston, 1902). In Edinburgh, there was a ward for emergencies "whether affecting patients already in the general wards or those living outside whose disordered mental state has not been fully confirmed" (Henderson, 1964). For a short period at the beginning of the 19th century, the Newcastle Infirmary tried to place patients according to the nature of their disease and other needs, so that "when a patient is apt to disturb others, he will be placed in separate rooms" (Poynter, 1964).

Attempted suicide was a criminal offence until 1961, but during the 19th century it appears to have been routine for those who unsuccessfully attempted suicide to be taken to the nearest hospital by their relatives, neighbours, or the police (Anderson, 1987). Most were discharged within a few hours, but others required admission for medical care; little attempt was made to assess psychological state, but the obviously suicidal were transferred to asylums or prison.

From the 1820s, psychological symptoms or puerperal fever and puerperal insanity were frequently noted in the records of lying-in hospitals and in the lying-in wards of general hospitals. Obstetricians accepted these conditions as part of their responsibility and described them in their textbooks; until this century, there was no suggestion that women should be transferred to fever hospitals or asylums (Loudun, 1988). Admissions to asylums for puerperal insanity all appear to have been from home weeks or months after delivery.

Alcohol was often mentioned as a cause of physical problems, and delirium tremens was one of the most frequent explanations for disturbed behaviour. Anorexia nervosa seems to have been an occasional cause of admission to medical wards, and may well have been a relatively common cause of wasting disorders (Parry-Jones, 1985).

Poor-law institutions

Workhouses provided for large numbers of the mentally ill and mentally deficient, including the certifiably insane (Abel-Smith, 1964). The Commissioners in Lunacy believed that workhouses, even those with infirmary wards, provided little medical and nursing care, and that they offered "far less physical comfort" with "far more personal confinement" (Hunter & MacAlpine, 1963). Conditions were often appalling: a special committee of the Huddersfield Guardians reported in 1857 that the lack of classification of those in hospital wards led to a deplorable mixture of cases, child and adult, physical and mental disorder, in "utterly unfit" accommodation (Marland, 1987).

During the 19th century a parallel system of general hospitals evolved from poor-law institutions. Acts of 1867 and 1868 clarified the duty to provide separate infirmaries for the sick. In some areas workhouses were converted, while others had separate infirmary blocks and in a few areas new infirmaries were built. Little has been written of their role in caring for the mentally disordered.

At the end of the century, some infirmaries began to admit non-pauper patients, and developed into municipal hospitals, but the workhouses and their infirmaries continued to provide most of the chronic institutional care for the elderly poor until 1948. Many of their patients suffered from dementia or affective disorder, but little effort was made to classify their psychiatric problems or needs (Townsend, 1962).

Developments in care 1890–1939

At the end of the 19th century, neurologists began to lose interest in conditions without a clear pathology, but few asylum doctors extended their interests beyond insanity. Sir David Henderson, Professor of Psychiatry at Edinburgh, later recalled that at that time, "the neurologist was an infinitely more acceptable member of the profession and the most nervous patients apart from those who were 'clearly off their head' were referred to him" (Henderson, 1964). However, Henderson was exceptional: he had spent two periods working with Adolph Meyer in the United States and was fully aware of the enthusiasm, in Europe and the United States, for the writings of Freud and his colleagues and for new psychological treatments (Taylor, 1988). He believed that he had benefited considerably from working for physicians at the Edinburgh Royal Infirmary, both on the acute disturbed ward and with Dr Alexander Bruce, who had a special interest in neurology and psychoneurosis. He noted, however, that:

> "the neurosis patients, almost irrespective of their particular diagnosis, were treated along the formal stereotyped lines advocated by Weir Mitchell.* They were confined to bed, screens isolated them from other ward patients, they were given a liberal milk diet, visitors were prohibited, and their psychotherapeutic treatment was based on suggestion, explanation, encouragement, and sympathetic understanding. Medicinal treatment consisted of tonics, bromides, and hypnotics at night time. The suggestive effects of this treatment were heightened by high-frequency electricity and ultra red/violet rays, which were credited with a virtue which they did not really possess. It became obvious that success in treatment depended then, as it does today, on the personality of the physician more than on the therapeutic agency employed." (Henderson, 1964)

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* Silas Weir Mitchell (1829–1914), Philadelphia physician and the foremost neurologist of his day, introduced and popularised the 'rest cure' for nervous disorder.

At the end of the century, some asylum doctors began to offer early and voluntary treatment of major psychiatric illness and of less serious disorders. Out-patient clinics were established within general hospitals, as were some in-patient units.

World War I had very considerable consequences for the understanding and treatment of the neuroses. From its beginning, large numbers of soldiers began to report the symptoms of what soon became known as 'shell-shock' (Stone, 1985). Research by the first cardiologists on another very common syndrome, 'soldiers' heart', also contributed to understanding of anxiety neurosis, which had recently been described by Freud (see Howell, 1985).

The main innovations in treatment, however, were made by neurologists and psychologists, many of whom had been influenced by the new ideas of psychoanalysis. The military authorities made relatively little attempt to obtain help from mental hospital psychiatrists. However, the Annual Report of Littlemore Hospital, Oxford, for 1917-18 recorded:

> "The Army Council, in agreement with the Board of Control took over Littlemore Asylum for shell-shock and neurasthenia cases during the World War. The whole of the existing asylum patients were transferred to other asylums, but offices and staff were retained to work in conjunction with additional medical and nursing staff appointed by the War-Office. The Asylum was handed over to the Military Authorities as a concern, took the name of the Ashurst War Hospital and ceased, for the duration of the war, to be an asylum."

Wartime experience of the management of mental disorder was soon reflected in textbooks and journals (Armstrong, 1980) and in clinical practice. In the 1920s and 1930s, many physicians emphasised psychological care; for example, Dr Varrier-Jones at Papworth Chest Hospital described his aims as being to "treat the patient, the whole patient, and his environment as well" (Bryder, 1988). Although some neurologists continued to be interested in the treatment of nervous disorders (Hurst, 1949), a new specialty of psychological medicine developed, both within the neurology departments of the voluntary hospitals and in private practice (*British Medical Journal*, 1936; Stone, 1985).

While many psychiatrists now accepted that neurotic problems could be severely disabling and they were best treated by psychological methods in general medical settings, asylum doctors generally rejected these ideas. The Report of the Royal Commission in 1926 and the subsequent Mental Treatment Act 1930 encouraged a greater role for the general hospitals and made voluntary treatment of major illness possible (Unsworth, 1987). Specialists in psychological medicine, the staff of the new Maudsley Hospital, and a few asylum doctors all helped to promote the academic status of psychiatry (Lewis, 1947; Hill, 1969; Shepherd, 1986), but resources were limited and general medical and public attitudes changed very slowly.

In-patient units

In the later years of the 19th century, a number of asylum doctors, especially in Scotland (MacLachlan, 1987), had argued the need for voluntary treatment of mental illness before it became severe enough to require admission to the asylum, the first published reference to this being by Gaskell in 1860 (Hunter & MacAlpine, 1963).

> "In Scotland in the middle and later parts of the nineteenth century many distinguished psychiatrists were . . . stressing the need for improved treatment and teaching facilities through the establishment of special wards in general hospitals." (Henderson, 1964)

The first general hospital unit opened in 1887 at the Barnhill Parochial Hospital, Glasgow, where Dr John Carswell carried out domiciliary visits and admitted 337 patients in the four years from May 1893. He concluded that "all cases of mental disease should be treated in hospitals or reception centres before being sent to asylums" (Henderson, 1964).

Carswell's experience provoked considerable interest, especially in Scotland. The value of early treatment was soon widely accepted, but there was no agreement as to whether this should be based in a general hospital, or a mental hospital site, or elsewhere. When Dr (later Sir) Thomas Clouston spoke to the Annual Meeting of the Medico-Psychological Association in 1902 on the need for "suitable means of treatment for incipient and transient mental diseases in our great general hospitals", the ensuing discussion was divided about selection, length of stay, and indeed the value and feasibility of such care. Although it was said that some general hospitals were already admitting psychiatric cases "pretty freely", some speakers thought that general hospitals lacked suitable facilities and nursing skills. Dr Savage stated that "the patients we see at Guy's had better not be there . . . I would rather see them in an asylum" (Clouston, 1902).

In-patient care in general hospitals during the early years of the present century developed in four forms: observation wards for emergency cases, units in teaching hospitals, the management of individual patients in general medical wards, and the use of out-patient clinics.

Observation wards

In 1904 the Glasgow City Corporation, which had been impressed by Dr Carswell's work at Barnhill Hospital, invited him to take charge of a 50-bed observation ward at Duke Street General Hospital (Henderson, 1964). Similar wards were established elsewhere in Britain following the Lunacy Act 1890, which consolidated previous legislation on emergency admission. Observation wards were mainly sited in poor-law hospitals, and aimed to provide initial assessment of mental illness as a preliminary to admission to a mental hospital. Little is known of how they operated, but the Board of Control (1935), describing a systematic examination of observation wards, found them "disquieting". Some wards were well equipped and had trained and experienced staff, but others had no facilities for assessment and no trained staff. Although the Board favoured the alternative of admission units at mental hospitals, a *Lancet* (1936) editorial took issue with this, claiming that the well-equipped and well-staffed observation unit could assess and treat many problems without the need for admission to a mental hospital.

A few general hospital observation wards also provided treatment, discharging many patients home rather than transferring them to mental hospitals. The few published descriptions mainly refer to wards provided by the London County Council, who were made responsible for the 20 London workhouses by the Local Government Act 1929. By 1939, their observation wards had been re-organised into six larger ones with 224 beds and trained staff; one was in a mental hospital, four were attached to general or geriatric hospitals, and one was in an undergraduate teaching hospital. The unit at St Francis Hospital (formerly the Constance Road Institution), Camberwell, was associated with the Maudsley Hospital, receiving weekly visits from Professor Mapother and, later, Sir Aubrey Lewis. It had a clear clinical policy and discharged many patients who did not require admission to a mental hospital (Pentreath & Dax, 1937; Eilenberg *et al*, 1962).

Teaching hospitals

The generally recognised need for improved training for psychiatrists led to the foundation of the Maudsley Hospital (which, after a period as an emergency hospital for shell-shock victims, opened as a postgraduate centre 1923) and to demands for in-patient units within larger general hospitals. Papers and editorials in the journals (see Jones, 1972; Baruch & Treacher, 1978), as well as the Report of the Royal Commission in 1926, argued that in-patient units within teaching and other general hospitals would be able to admit interesting cases for the benefit of medical students and of psychiatrists in training. The lack of progress in Britain was often contrasted with developments in the United States, where the Rockefeller Foundation endowed several large teaching units during the 1930s, and where there were 40 general hospitals by 1940 (Greenhill, 1979; Lebensohn, 1980).

From 1918, the Board of Control repeatedly called for teaching wards in general hospitals. Its 1931 Annual Report reviewed the implications of the Mental Treatment Act 1930 and stated that such "provision is important particularly in relation to borderline cases" of mental illness and also for mental conditions complicated by physical disorders. The Board believed that the number of psychiatric patients in non-teaching hospitals should be small and that:

> "It is far more important that the teaching hospitals should take advantage of the Act, because of the value to students in extending their range and variety of the clinical material. We look forward to the time when the larger teaching hospitals will have a complete psychiatric unit attached, such as forms part of the medical centre of Columbia University. This is an ideal which it may take years to realise, but in the meantime we regret that hitherto voluntary hospitals have not shown any readiness to take advantage of the new opportunity".

Enthusiasm and official encouragement did not result in achievement. The first teaching hospital unit, the only one before World War II, was that at King's College Hospital, where a 35-bed ward was allocated to Professor Mapother and staffed by the Maudsley Hospital. Mapother was soon convinced that the success of this experiment was "no argument whatever" for the general theory of admitting mental cases to general hospital wards:

> "all experience derived from this ward supports the view that only under the special conditions of association with a psychiatric clinic that a single ward in a general hospital can properly deal with truly recent cases of mental and even neurotic disorder." (see Lewis, 1969)

It closed on Mapother's retirement in 1939. A 35-bed unit was planned for St George's Hospital, but these plans were abandoned on the outbreak of war.

Beds in general wards

In the inter-war years, both before and after the 1930 Act, a number of hospitals allowed psychiatrists and their staff to admit to general medical wards. Passing references to these were made by individual psychiatrists (Board of Control, 1922, 1930; Baruch & Treacher, 1978), and the Board of Control Report for 1930 listed several hospitals with psychiatric beds. Two of the London teaching hospitals, Guy's and the Middlesex, each allocated six beds for psychiatry (*Lancet*, 1938). Dr Gilmour, Medical Superintendent of St Luke's Hospital, found that it was possible to treat a wide variety of serious psychiatric problems in its beds, with an average length of stay of three months (Board of Control, 1930).

Out-patient clinics

Dr Rayner, formerly Superintendent of Hanwell Asylum, opened the first general hospital clinic at St Thomas's Hospital in about 1890. Four London teaching hospitals, Guy's Hospital, Charing Cross, St Mary's and University College Hospital (UCH), as well as several hospitals outside London, opened out-patient departments before 1914. The first in Scotland, and probably the first established by a mental hospital psychiatrist, was inaugurated at the Western Infirmary, Glasgow, in 1910, by Dr Oswald, Superintendent of Gartnavel Royal Asylum. By 1915 Dr Hubert Bond, a medical commissioner at the Board of Control, could tell an audience at the Middlesex Hospital that "I can see no reason why outpatient clinics should not be established in connection with every hospital in the country" (Bond, 1915).

In the years following World War I, further out-patient departments opened, partly as a result of concern on the part of the Ministry of Pensions about the continuing care of chronic shell-shock patients. Most of these new clinics were attached to voluntary hospitals, were independent of the asylums, and were staffed by doctors who regarded themselves as physicians in psychological medicine. However, a few hospitals appointed to them psychiatrists who were already on the staff of mental hospitals: perhaps the earliest of these in England was the Physician Superintendent of Littlemore Hospital, Oxford, Dr T. S. Good, who became an honorary physician in the Department of Nervous Disorders at the Radcliffe Infirmary, Oxford, in 1918. This weekly clinic developed from the wartime unit for shell-shock, established by the neurologist Sir Arthur Hurst (Hurst, 1949) and by the psychologist William McDougall, and was intended for the treatment of patients with early symptoms of psychiatric disorder (Board of Control, 1922, 1930). A history of the hospital (Gibson, 1963) later recorded that "each patient receives a thorough overhaul of his nervous system", and claimed "this department is a most important factor in lessening the incidence of mental disease in the city and district".

Most physicians in psychological medicine were influenced by developments in psychoanalysis, and treated neurotic patients referred from other hospital clinics or from general practitioners. The principal treatment was psychotherapy, together with advice and help from psychiatric social workers and occasionally of psychologists (Blacker, 1946). Several of these physicians, e.g. Bernard Hart, at UCH, London, were pioneers of psychotherapy; however, resources were minimal and, at UCH, "interviewing of outpatients took place in the (lighted) darkroom in the eye department" until, after World War II, the clinic moved to the basement of the obstetric hospital (Merrington, 1976). Few cases of psychotic disorder were seen in these clinics, and those that did attend "were often dealt with by recommendation that they be brought to the attention of the relieving officer" (Blacker, 1946).

Throughout the inter-war years, the Board of Control (1922, 1930) encouraged the setting up of clinics for new referrals and after-care. Its 1919 Annual Report stated that:

> "the establishment of psychiatric clinics attached to general hospitals or to institutions otherwise, which is inseparably connected with an improvement of the methods of dealing with the incipient sanity, has continued to excite general interest and practical discussion. This has been the case particularly at certain important university centres where the municipal, the professional and the teaching element are eager to inaugurate the better system as soon as conditions allow."

Although, in 1930, there were still only 29 out-patient clinics in Britain (Blacker, 1946), the Mental Treatment Act 1930 gave local authorities the power to arrange out-patient treatment, and resulted in the opening of many more clinics, so that by 1942 there were at least 216. Dr Duncan MacMillan (1965), of Mapperly Hospital, Nottingham, described how he was seconded to the Maudsley Hospital to learn about the out-patient treatment of neurosis, before setting up a three-weekly clinic in a rented room at the local general hospital. However, the Board of Control remained concerned that many areas of Britain had made no effort to provide out-patient care, and that many clinics were infrequent and perfunctory. In the face of some criticism from mental hospital doctors, they insisted that there could be, and should be, a role for other psychiatrists in out-patient departments.

During World War II, at the instigation of Sir Aubrey Lewis and with the support of the Ministry of Health, Dr C. P. Blacker surveyed the out-patient treatment of neurosis, in order to provide a basis for recommendations for post-war plans. Of 210 clinics in England and Wales that provided information, most (83.1%) had been founded since 1930, 71% were located in voluntary hospitals, 14.3% in minicipal hospitals, 7.1% in mental hospitals, and 7.6% in other places. Most of the longest established clinics were independent of mental hospitals, but of the much larger number set up since the 1930 Act, most were staffed by mental hospital psychiatrists. Blacker (1946) found that the independent clinics were much better staffed, saw more new patients, had more regular clinics and dealt with higher proportions of neurotic patients.

Developments in care 1939–60

At the end of the 1930s, the mental hospitals were overcrowded and understaffed: they were isolated from other medical care, and despite individual exceptions, had failed to respond to the opportunities or to the new treatments and to limited opportunities offered by the Mental Treatment Act 1930 (Webster, 1988). World War II, like World War I, had very considerable consequences for psychiatry – this time, a radically new approach to mental illness and the introduction of the National Health Service (NHS).

Wartime experience in emergency hospitals and of the treatment of neurotic conditions had in fact changed medical views on the scope and methods of psychiatry. Psychological treatment became generally more acceptable, and the physical treatments now offered medical answers to illnesses that had previously been dealt with only by chronic institutional care. Plans for the NHS disregarded the arguments of the Board of Control for a separate mental illness service, combining services for the mentally and physically ill in a single administrative structure (Webster, 1988), while teaching hospitals were given a separate status. Changing clinical practice and more enlightened public attitudes were later reflected in the 1957 Royal Commission on the law relating to mental illness and mental deficiency, and were partly embodied in the Mental Health Act 1959 (see Unsworth, 1987).

Influential specialists in psychological medicine, such as Sir Aubrey Lewis, saw psychiatry as a medical specialty which should have a substantial presence in teaching hospitals and in other large general hospitals. These views were reflected in editorials in the *British Medical Journal* (1945) and in the *Lancet* (1937, 1938) and in the tripartite report of the Royal College of Physicians, the British Medical Association and the Royal Medico-Psychological Association (RMPA) (1945). There was general agreement about the educational need for psychiatry in teaching hospitals, but a wider role of general hospital units was rejected by some mental hospital doctors, who believed that reformed asylums offered a more appropriate therapeutic setting (see Jones, 1972; Baruch & Treacher, 1978).

The NHS did not result in any increase in resources. Indeed there was an actual decrease, compared with before the war, and mental disorder had a lower priority than physical illness. The lack of new buildings and of skilled staff (especially nurses), in the face of rising demand, inevitably resulted in low morale and in declining standards of mental hospital care (Webster, 1988). In the mid- and late-1950s, planning for new capital spending on mental hospitals began, just as a decline in in-patient numbers was becoming apparent. General hospital psychiatry seemed to many psychiatrists and planners to be the economic and the clinical answer (Baruch & Treacher, 1978; Jones, 1972).

Teaching hospitals

Teaching hospitals, both on their own initiative and in response to pressure from the Goodenough Committee on Medical Education (1944), the University Grants Committee, and the General Medical Council, slowly began to provide limited facilities for teaching psychiatry to students (Lewis, 1947; Hill, 1969). The first in-patient department was at Guy's Hospital, London. Before the war, Dr R. D. Gillespie, physician in psychological medicine, had been given a large anonymous benefaction, which he brought to Guy's for a department of psychiatry. The York Clinic opened with 45 beds in 1944, initially as an emergency medical service hospital for officers, and then with a mixture of private and public beds. Dr David Stafford-Clark was appointed to the staff in 1950 and an active department of psychological medicine was developed which provided acute treatment, out-patient services, and consultations both on general wards and in the casualty department (Brook, 1964; Stafford-Clark, 1965).

Other teaching hospitals also expanded their departments of psychological medicine. Dr William Sargant was appointed at St Thomas's Hospital; he was allocated a basement bedstore and wartime shelter, nick-named 'Scutari', which he converted into an out-patient treatment unit; in 1951, a 20-bed in-patient unit was opened in the nearby Royal Waterloo Hospital. St Thomas's rapidly became known for its vigorous use of the new methods of physical treatment, and Sargant later said that "I was at that time very keen to show that psychiatry, in its new and varied treatment aspects, did not seem to me to be really very different from general medicine" (National Association for Mental Health, 1961). At St George's Hospital, Dr Desmond Curran (1963) returned after the war to find that the 1930s' plan for a 30-bed in-patient unit had been indefinitely postponed. He was, however, given 46 beds and a house to be used for an out-patient department at Atkinson Morley's Hospital, seven miles from the main site.

Before the war, there had been only two university departments of psychiatry (at Edinburgh and the Maudsley), but between 1948 and 1960, eight provincial clinical schools created professorial departments (Lewis, 1947; Hill, 1969). Many were small; Manchester, for instance, began in 1949 with only eight beds, divided between two medical wards. The academic unit at the Middlesex Hospital, which opened in 1961 with 15 beds (together with 70 at St Luke's), was the first in London, and its first professor, Sir Denis Hill, placed a special emphasis on consultation and liaison services to the rest of the hospital (Crisp, 1968; Hill, 1969).

Despite the efforts of a small number of academically minded psychiatrists, a survey in 1962 on behalf of the Psychological Medicine Subcommittee of the Royal College of Physicians showed a "shocking situation, with few psychiatric beds in teaching hospitals and only a modest number within easy reach" (Curran, 1963). None of the academic and teaching hospital departments had local responsibilities, and few wanted them. In Lewis's view (1947), "it is now well understood that it is the duty of the teaching unit to select cases for its particular needs rather than to accept all and sundry," but Curran (1963) disagreed, and in a Presidential Address to the RMPA, said that selection made assessment and management difficult and was an unsatisfactory basis for teaching medical students. It was only with the abolition of the separate status of teaching hospitals and their boards of governors, however, that teaching hospitals took on catchment area responsibilities.

Out-patient services

In the years after 1948, many new general hospital clinics were founded. Dr Henry Rollin (1990) has described the experiences of a London mental hospital psychiatrist. He became a consultant at Horton Hospital in 1948, and set up an out-patient clinic at St Stephen's Hospital, in the Horton catchment area, for both new and follow-up patients; resented and unwanted by the St Stephen's staff, he worked in a linen room, keeping his records in a shoebox. Arbitrary changes in the catchment area meant that he had to move on to set up clinics in several other general hospitals. At New End Hospital, Hampstead, there was a weekly clinic which received new referrals both from other hospital departments and from general practitioners, as well as offering care to those discharged from Horton; here, there were good working relationships with other members of hospital staff.

In-patient units

The value of non-teaching general hospital units was vigorously debated during and after the war (Jones, 1972; Baruch & Treacher, 1978). Academic psychiatrists made unfavourable comparisons with other countries, especially the United States, where between 1940 and 1963 the number of general hospital departments grew from 40 to about 500 (Greenhill, 1979; Lebensohn, 1980). In contrast, a number of mental hospital doctors pointed to the success of their reforms, and argued that they could provide more skilled and sympathetic care.

In 1948, the new Manchester Regional Hospital Board rejected proposals for new mental hospitals, and took the lead in developing psychiatric units within general hospitals (Pickstone, 1989). Important local factors behind this decision were unsolved problems of the region's large mental hospitals, which had been beset by pre-war scandals, and the existence of numerous county boroughs with populations of around 250 000, each of which already had observation wards within their ex-workhouse general hospitals. The medical members and administrators at the regional board took advantage of these opportunities to create a new pattern of care. Another factor which later became important was the belief that services could be provided more cheaply in general hospitals (Kessel, 1973). During 1948–55, the Manchester region was a notably low-spending one, devoting only 20% of its capital allocation to the mental illness sector, compared with 30% by the neighbouring Newcastle and Sheffield boards (Webster, 1988).

Planning began in 1948–49 and observation wards then began to be transformed into treatment units, with newly appointed staff. Four units were large enough to hope to offer a comprehensive service (Burnley, Bolton, Oldham, Blackburn), the remainder of the 11 units established by 1960 being initially rather smaller. Most psychiatrists had expected that these units would soon be overwhelmed by patients requiring long-term care, but this was not so.

The enterprise and enthusiasm of the staff of these new services are very impressive, but they almost certainly overstated their achievements (Leyberg, 1959; Silverman, 1961; Hoenig & Hamilton, 1969; Hill, 1969; Freeman, 1983, 1984). According to Freeman (1983), who developed the Salford service:

> "The claim that these units dealt with *all* cases of psychiatric disorder in the catchment area requiring specialist attention raised questions about the boundaries of psychiatric responsibility which were never adequately faced."

Some units had only one consultant for populations of around 200 000, while there were few other medical staff and very few social workers or psychologists. Only the severely ill could be treated and there was little opportunity for psychological methods. The services were cheap and bed usage was remarkably low. Although the standard of care was comparable with that of the old mental hospitals (Hoenig & Hamilton, 1969), such a standard was satisfactory only in terms of the low expectations of communities who had known nothing better (Kessel, 1973).

General hospital units developed less quickly in other areas of Britain, and by 1960 there were 82, half of these with less than 25 beds (Rehin & Martin, 1963); most of them developed from observation wards, but a few were entirely new. In addition, some general hospitals allowed a small number of psychiatric admissions to general medical wards (Brook & Stafford-Clark, 1961).

The 1962 Hospital Plan and after

The problems arising from the lack of investment over many years, including the early years of the NHS, were finally tackled in the 1962 Hospital Plan, which based services on district general hospitals. This adopted a model proposed by Professor Thomas McKeown in which district hospitals were to provide the whole range of medical services for defined local communities (Cawley & McKeown, 1963).

In March 1961, the Minister of Health, Enoch Powell, spoke at the Annual Conference of the National Association for Mental Health, and presented a strikingly phrased account of the implications for the forthcoming mental illness services. He noted recent statistical predictions of a continuing decrease in beds, and stated that "we should rather err on the side of underestimating the provision which ought to be required in hospitals 15 years from now" (National Association for Mental Health, 1961). These beds "ought for the most part to be in wards and wings of general hospitals. Few ought to be in great isolated institutions or clumps of institutions," and he looked forward to "nothing less than the elimination of by far the greater part of this country's mental hospitals as they exist today". The minister rejected alternative uses for mental hospitals: "if we err, it is our duty to err on the side of ruthlessness". The resistance of those who had devoted themselves to working in mental hospitals and lack of resources had to be overcome. It was the duty of any minister of health "to choose and to favour wherever they have the choice, the course of more drastic and fundamental change".

The Ministry of Health Memorandum "Planning of Hospital Services for the Mentally Ill", published a few days later, was more subdued, being relatively cautious about the precise predictions of bed needs and implying a continuing role for mental hospitals, particularly for long-stay patients. The 1962 Hospital Plan itself again stated that it would usually be desirable to treat short-stay patients in units attached to general hospitals and that this would allow the closure of a large number of mental hospitals. The regional details included in the plan outlined changes which were a great deal less revolutionary than the minister had implied. Only 20 of the 130 mental hospitals were to be closed by 1975, and the projected percentages of beds in general hospitals by then ranged from 24% to 3%. The Plan lacked details of costings, and recommended community care without considering its funding or organisation (Freeman, 1983). It was notable that the Scottish plan was considerably more cautious.

The origins of the emphasis in the Hospital Plan on general hospital psychiatry are not entirely certain. The reduction in the numbers of people in mental hospitals was by then clearly established, while the asylums were old, decrepit, and often sited far away from where their patients lived. New physical and psychological methods of treatment had generated great optimism, and there was a widespread belief that psychiatry should be closer to other medical disciplines. For a number of years the Ministry of Health had been taking an interest in general hospital units in North America and especially in developments in the Manchester region (Freeman, 1988*a*). Reports of the Chief Medical Officer had increasingly stressed both their importance and the need to avoid new investment in the expansion or rebuilding of mental hospitals (Freeman, 1983, 1984, 1988*a,b*).

On the other hand, by then, there had been no systematic descriptions or evaluations of any of the 82 general hospital units established by 1960, most of which were fairly small. It seems fairly certain that economic considerations contributed to the radical nature of the Hospital Plan: it was essential to find ways of modernising services at the cheapest cost (Rehin & Martin, 1963), since changes in the care of mental illness were but one part of a long overdue rebuilding programme for hospitals in general.

Thus, a vigorous minister of health was able to transform a slowly developing strategy into a new political initiative (Freeman, 1988*a,b*). The Hospital Plan resulted in immediate controversy, in part about the desirability of psychiatric care in general hospitals, and in part about the dangers of developing two separate services in which the mental hospitals might be left with the most difficult patients but with fewer resources and staff, and less status (Jones, 1972). Rehin & Martin (1963) cogently summarised the implications of the Plan, as well as the advantages and disadvantages of general hospital care. The advantages would be the accessibility of general hospital units, the availability of the general hospital's, medical and other specialist services, and reduction of the stigma of mental illness. Disadvantages would be difficulties in coping with more difficult and long-stay patients, and the problems of establishing and administering a psychiatric unit within a general hospital which would be unfamiliar with the needs of the mentally ill. Rehin & Martin (1963), criticising the absence of guidance on selection of patients for general hospital units and on the management of the medium-stay and long-stay patients, concluded that "the literature on general hospital inpatient psychiatry is neither extensive nor very rigorous methodologically and provides no solid foundation upon which to build a plan".

Developments since 1962

Accounts of general hospital units in the 1960s and early 1970s described varied services, some attempting to provide a comprehensive service for a catchment area, and others treating small numbers of selected patients of good prognosis. Some encountered difficulties in treating psychiatric patients in uncomprehending general hospitals, while others made extreme claims of the ability of small units to provide psychiatric care without the need of any back-up from a mental hospital. Reviewing early experience, Martin & Rehin (1969) were pessimistic as to whether a truly comprehensive general hospital psychiatry would be possible in more than a minority of hospitals.

Criticisms of the way in which district general hospital units were established should not be seen as denying their fundamental, and even self-evident value (Kessell, 1973). However, it is disappointing and unsatisfactory that we still do not know how they can be most effectively sited and run. Little has been written in the last 15 years, and national policies have only slowly admitted the relevant problems or the need for flexibility. There was some recognition in the 1975 white paper (Department of Health and Social Security, 1975), but official reservations were only made explicit in the 1985 reply by the DHSS to the Report of the House of Commons Social Services Select Committee (Department of Health and Social Security, 1985).

Newer departments have avoided some of the mistakes of early units, and there has been increasing emphasis on specially designed buildings on general hospital sites, but separate from them. It appears increasingly that by far the most important determinant of the working of a general hospital unit is the clinical policy of the consultants (Mahadevan & Foster, 1982), and despite the acerbity of the arguments, it is still not clear that there is necessarily any very great difference between a district general hospital unit in the grounds of a general hospital and a small conveniently sited mental hospital.

It is regrettable that there has been little adequate evaluation of general hospital units. Early accounts lack detail, fail to compare like with like, and give no convincing support to the decision that general hospital units should replace the mental hospitals (Jones *et al*, 1980). Although cost–benefit studies in the Manchester area have suggested considerable clinical and academic advantages for general hospital units, they also confirm the minimal resources allocated to them (Jones *et al*, 1980; Goldberg, 1980).

Consultation and liaison

Until the Mental Health Act 1959, certifiable disturbed patients in general hospitals were usually transferred to asylums on the authority of the relieving officer (renamed the duly authorised officer in 1948), without a psychiatrist being involved. Many of the referrals of neurotic problems to the early out-patient clinics were from other hospital departments (*Lancet*, 1937), but we know little of the extent of consultation on medical and surgical wards in the first half of the 20th century.

There are a few references to specialists in psychological medicine and to mental hospital psychiatrists who had out-patient or teaching commitments seeing ward consultations. Henderson (1964) described attending the delirium ward at the Edinburgh Royal Infirmary, senior doctors can recall seeing psychiatrists on the wards of pre-war teaching hospitals, and Macmillan (1965) described how, in the 1930s, his Nottingham out-patient clinic expanded to take on ward consultations and to see all cases of attempted suicide.

After World War II, and especially after 1948, consultation became more firmly established, either as informal referrals to individual psychiatrists or by requests to duty doctors. The Mental Health Act 1959 made it essential to involve psychiatrists in any transfer to a psychiatric hospital. Rollin (personal communication) remembers seeing some requests before and after his general hospital out-patient clinics. Professor Max Hamilton (personal communication) found that, as a registrar at UCH, he had no specific duties of that kind, but that "taking my lunch occasionally with other registrars, it gradually filtered around the hospital that I was available. In the course of time, I was being requested to see patients in Casualty and being invited to medical and surgical wards, and eventually to the obstetric hospital." A few hospitals began more organised systems. Dr Stafford-Clark established a service at Guy's (Fleminger & Mallet, 1962), and Professor Michael Shepherd supervised Maudsley senior registrars at Dulwich Hospital (Kenyon & Rutter, 1963).

A more elaborate liaison service was established in 1961 at the Middlesex Hospital by Sir Denis Hill and his colleagues modelled on the system developed at Rochester, New York, by Romano and Engel, in which psychiatrists had liaison attachments to individual medical units (Crisp, 1968; Hill, 1969).

Attempted suicide has accounted for a substantial proportion of the cases referred in descriptions of consultation services published since 1960. However, until the 1950s, hospital cases of attempted suicide were rarely seen by psychiatrists, and indeed, the clinical characteristics were not defined until the publication of a monograph by Stengel & Cook (1958). Within a few months of the abolition of suicide as a criminal offence, the Ministry of Health (1961) published a circular recommending that "all cases of attempted suicide brought to a hospital receive psychiatric investigation before discharge". The advice was followed by a report on the treatment of poisoning in 1962 and by that of a committee on the same subject, chaired by Sir Denis Hill, in 1968 (Ministry of Health, 1968). Stengel (1963) found the initial advice impractical, in view of the numbers, and few hospitals managed to follow it. Edinburgh changed its delirium ward into a poisons unit, run by physicians but with psychiatric consultation (Kessel, 1965; Kreitman, 1977). Oxford developed a service staffed by non-medical counsellors, while Cambridge trained medical staff to carry out routine psychological assessments (Hawton & Catalan, 1987). The success of these services and the impracticality of the official advice in face of increasing numbers was recognised in new DHSS guidelines, developed in consultation with the Royal College of Psychiatrists (Department of Health and Social Security, 1984).

Consultation and liaison has now become an established and popular special interest of both general and child psychiatrists, but there are very few full-time liaison psychiatrists, and overall practice remains haphazard (Mayou & Lloyd, 1985). Many hospitals have to rely on either informal referrals or duty psychiatrists.

Conclusions

General hospital psychiatry has had a long history, but one that has been neglected by both historians and psychiatrists. In the 20th century, the care of major mental illness has returned to the general hospitals. It has done so for compelling educational and clinical reasons, but in a manner determined as much by economic expediency as by clinical evidence. It is now being practised in many different ways, and requires proper evaluation.

Changes in the siting of specialist psychiatric care have been accompanied by an expansion of the boundaries of psychiatry to include emotional and behavioural disorders which were formerly seen as the responsibility of physicians and neurologists. These boundaries remain uncertain and require definition in the general hospital as much as they do in general practice.

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Physical Health of the Long-Term Mentally Ill in the Community
Is There Unmet Need?

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A clinical assessment was made of 145 long-term users of hospital and social-services day psychiatric facilities, and 84 consented to laboratory pathological screening. We recorded data on relevant medical care where that was being provided. Based on clinical assessment, 59 patients (41%) were judged to have medical problems potentially requiring care. Based on pathological screening 39 (44% of those assessed) had unmet needs, and this rating was associated with poor compliance with attendance and treatment plans. Altogether, 12 patients had important unmet needs, mainly for detailed medical investigation, although none required immediate hospital admission. Long-term patients should be medically reassessed and supervised at appropriate intervals.

A central feature of current psychiatric service plans and practice in most developed countries is the transfer of long-term, chronically handicapped psychiatric patients from hospital to dispersed, community-based facilities (Department of Health and Social Security, 1975; Brugha *et al*, 1988). This decentralisation of care could result in reduced clinical supervision of a vulnerable population, with a consequent increase in untreated physical morbidity. Epidemiological surveys have frequently demonstrated the existence of an excess of physical morbidity and premature mortality in both treated and untreated populations of the mentally ill (*Lancet*, 1979; Andrews *et al*, 1977). The purpose of our survey was not only to identify the amount of physical morbidity in a population of long-term community psychiatric service users, but also to assess their unmet needs for medical care by considering their problems in relation to information about their current clinical management, in a well resourced health district. We defined medical care as the investigation, supervision, or treatment of physical illness or disability. We hypothesised that we would uncover a considerable amount of unmet need for medical care in association with two factors: (a) a rating of poor compliance with treatment and irregular attendance and (b) location at a social-services (non-hospital-based) day psychiatric facility.

Method

The survey formed part of the Camberwell High Contact Survey (CHCS; Brugha *et al*, 1988); consent to participate in the survey was obtained from 145 men and women aged 18 and over, residing in a defined area (South Southwark), who were continuously in contact with specialised psychiatric services for 12 months, and who were attending a day psychiatric facility for at least one weekly session. Patients with severe mental retardation or a record of primary substance misuse, and those aged 65 or over who were suffering from dementia, were excluded. Patients were interviewed by a research psychiatrist concerning psychological and physical complaints, weight, cigarette smoking, dental care, drug treatment, and recent clinical investigations. Any observations concerning possible physical disease were recorded, and the patient's psychiatrist was asked to complete a questionnaire about known physical illness and personal health care. All psychiatric case notes were examined and details of other clinical investigations were recorded. Staff at the psychiatric facility and any relatives in close contact with the patient were interviewed about psychological, behavioural, and physical problems, and about all current treatment being provided. A procedure for rating need for care was applied, the MRC Needs for Care Assessment (Brewin *et al*, 1987), which used a combination of data on problems and treatment to rate medical problems requiring care and whether these were met.

Patients were also asked to agree to a blood sample being taken for a pathology screen. Blood samples were analysed for the following: urea and electrolytes, ESR, blood count, red cell volume, thyroid and liver function tests, protein and albumin, vitamins (folate and B_{12}), glucose and glycosylated haemoglobin and VD serology. The test results were examined and a judgement made in each case by two of the authors (TSB and BLS) of whether a need for medical investigation or treatment existed and of whether that need was currently met. Unless an abnormal test result was consistent with an existing known and treated condition, it was regarded as a need that was also unmet. Unmet need was rated as such only when a test result deviated significantly from the laboratory reference range (details of which are given in the footnotes to Table I). For example, we were seriously concerned where a serum creatinine level above 120 μmol/l (reference level 33–100) was discovered, unless it was consistent with a condition known to the patient's doctor and, as far as possible, was being appropriately managed.

CALCUTTA CENTRAL

TABLE I

Details of 12 cases where unmet needs for medical assessment or treatment were found

Case No.	*Sex of patient*	*Age*	*Psychiatric diagnosis*[1]	*Contact*[2] *years*	*Clinical/pathological problems*[3]	*Possible or established physical diagnosis*	*Medical investigation or care*	
							Provided currently:	*Unmet need for:*
1	F	51	Paranoid psychosis	34	TSH 7.8/Alk.P. 137; dental/gum disease	?Pre-clinical hypothyroidism; ?osteoporosis	None	Assessment by physician; dental assessment
2	F	39	Manic depressive	13	Post-traumatic retinal detachment; path screen: normal	Visual impairment	None	Ophthalmic assessment
3	F	30	Manic depressive	7	AST 49/Alk.P 121/GGT 37/ neutrophils 1.6	Hepatic disorder; ?drug or alcohol induced	None	Assessment by physician
4	F	54	Manic depressive	10	Complaining of tiredness; $T_4 = 12$/ free $T_4 < 2$/TSH 26/AST 62/Creat 125	Marked hypthyroidism (?due to lithium)	None	Assessment by physician
5	M	35	Schizophrenia	13	Haemoptysis; Alk.P 129/WBC 12.5	Respiratory infection; unexplained haemoptysis	Antimicrobial regime	Assessment by physician/ thoracic surgeon
6	M	75	Paranoid psychosis	2	Impaired hearing; path screen within age-adjusted normal range	Post mastoidectomy; impaired hearing	None	ENT assessment; hearing aid
7	F	32	Psychotic depression	10	Severe dental/gum disease; obesity; path screen: refused	None known	None	Dental assessment; advice on diet
8	M	44	Schizoid personality/ mild autism	27	No complaints; denies alcohol abuse; HbA$_1$C 7.2%/Glucose 9.2/ AST 48/GGT 56	?Alcohol or drug-induced hepatic disease; ?diabetes mellitus	None	Assessment by physician
9	M	51	Paranoid psychosis	27	Complaint: poor energy, chest pain; Fe 10/Fol 1.8	Known case of beta thallasaemia minor	No recent medical care	Increased medical supervision
10	F	51	Personality disorder	30	Complaint: fluid discharge from ear; history: tympanic perforation; path screen: normal	?Inadequately treated otitis media	No recent medical assessment	Otolaryngology assessment
11	M	73	Schizophrenia	55	Complaint: difficulty in chewing and swallowing food; refused dentures; Hb, PCV and Fe borderline low levels for age	?Dietary iron deficiency anaemia	None	Medical assessment; close monitoring of weight and food intake
12	M	43	Nil	26	Disabled by unpredictable myoclonic jerks; Alk.P 144/GGT 140/Fol 0.8	Known myoclonic epilepsy; drug-induced folate deficiency	Regular medical supervision and treatment	Coping advice for patient and his wife

1. Psychiatric diagnosis = most severe lifetime episode.
2. Contact = years since first contact with psychiatric services.
3. Pathology screen reference levels (SI units): TSH (thyroid stimulating hormone), mU/l (0–7); Alk.P (alkaline phosphatase), IU/l (20–100) (see text); GGT (gamma glutamyl transferase), IU/l (male 4–35, female 2–25); Creat (serum creatinine), μmol/l (33–100) (see text); HbA$_1$C (glycosylated haemoglobin), 3–6%, *borderline* 6–7%; Fol (serum folate), μm/l (2–14); AST (aspartase transaminase), IU/l (7–40); T_4 (serum free thyroxine), pmol/l (10–28); WBC (white cell count), $\times 10^9$/l (4–11); Fe (serum iron), μmol/l (male 13–26, female 11–22); PCV (packed cell volume), male 0.400–0.540, female 0.350–0.470.

Results

Personal health

Of 121 attenders from whom satisfactory information was obtained, excess weight, according to the height–weight index (Royal College of Physicians, 1983), was found in 49%. About a quarter of the members of the series smoked more than 20 cigarettes a day. A simple global rating of the presence of dental or gum disease was made in 28% of those who were examined; severe problems with dental hygiene, however, were less common and were found in 11 attenders.

Physical health problems

Satisfactory clinical information from the patient's own doctor was unobtainable in 28 cases, but with data from other sources, a physical problem requiring medical care (or clinical investigation) could be rated in all but one case in the series.

Fifty-nine were judged to have a physical health problem. More than half (52%) of those aged 50 or over had such a problem, compared with 28% of attenders under 50 (95% confidence interval for difference in proportions = 9–40%). However, there was no association between this rating and the patient's sex, psychiatric diagnosis, type of day setting attended or compliance with treatment plans.

In 49 of the 59 cases this clinically identified problem was rated as a met need: eight had hypertension, six diabetes mellitus, five hypothyroidism; there were four cases each of chronic obstructive airways disease and poor hearing and three cases of epilepsy. There were five cases each of other neurological, cardiovascular and locomotor system disorders, and two each of urinary tract and dermatological disorders. There were six other problems, of which two were cases undergoing investigation for unexplained abnormalities.

In 84 cases patients agreed to provide a blood sample either when interviewed or by arrangement with their own psychiatrist (the latter occasionally providing test results obtained routinely in the previous three months). A careful search for results on the remaining patients was carried out in the local hospital laboratories and in only four additional cases were further results obtained that had been carried out within 12 months of the interview. We are satisfied that the remaining patients were unlikely to have had pathology investigations during the previous year. Of the 88 patients, 39 (44%) were rated as having a problem requiring investigation or treatment, identified by the pathology screen. These patients were more likely to have failed to comply with attendance plans or with recommended treatment ($\chi^2 = 5.77$, 1 d.f., $P < 0.05$). Patients with problems identified by the laboratory screen were more likely also to have a problem based on the clinical assessment ($\chi^2 = 4.07$, 1 d.f., $P < 0.05$). Apart from these relationships, there was no other association between the presence of such a problem and any other possibly relevant factor such as age, sex of patient, attendance at a non-hospital day psychiatric service or the patient's psychiatric diagnosis.

Nine cases of problems, identified by the laboratory screen, were due to abnormalities already known to be present (e.g. hypothyroidism, diabetes mellitus) and were being dealt with satisfactorily. Another 25 cases were judged to be slightly abnormal results that were not thought to be urgent but ought to be followed up with repeat investigations by the patient's own family doctor or psychiatrist, before considering the need for more specialised investigations. They included eight cases with depressed white blood cell counts that could have been drug induced, nine with elevated alkaline phosphatase levels, four with elevated blood urea or creatinine or both, and two known diabetics with elevated blood glucose levels that might indicate inadequate control. Thus the laboratory screen did demonstrate problems in 39 cases but unmet need was rated in only five of these.

Unmet needs for care

Table I provides details of 12 cases where at least one need was rated as unmet on the basis of one or both assessments. Of ten cases where there were clinically identified unmet needs, one case was regarded as relatively unimportant and is not included in the table. The five patients with unmet needs identified by the laboratory screen were judged to require immediate medical investigation by an appropriate hospital consultant, although no case was sufficiently urgent to require the patient's admission to hospital. Two patients were rated as having unmet needs on the basis of both the clinical and the pathological assessments.

Two patients with unmet needs identified by the pathology screen had undetected hypothyroidism (both cases were subsequently confirmed). Altogether, only two patients had unmet needs for treatment, the remainder requiring specialised medical investigation.

Discussion

In our survey of long-term psychiatric patients in regular contact with day services, 41% had clinically identifiable problems requiring medical care, of which 15% were unmet needs. Although the responsible physician had apparently usually known of these unresolved problems in the past, none was receiving the attention that we judged was required. A laboratory pathology screen successfully carried out on 61% of the sample showed that 44% of those assessed had problems, of which 13% ($n = 5$) were unmet needs (Table I) despite their all being judged to be in urgent need of care (for assessment by a hospital specialist).

Two sets of pathology screening tests appeared to be particularly useful: thyroid function tests and liver function tests. We rated as abnormal only those thyroid function tests which were outside the reference range (Table I), on the basis of population studies performed by Amersham International Ltd, and used in their literature, which meet FDA regulations for clinical reagents. These reference ranges were also confirmed in our own laboratories. Similarly, the reference range for alkaline phosphatase was confirmed by our own laboratories (and also by King's College Hospital, London), which agree with ranges published at the time of the survey (Gidlow *et al*, 1983). In 1987 one of us (BLS) screened blood donors and confirmed a normal range of up to 98 for this test. To prevent false positive results we set a conservative upper limit of 130, and in older patients 140 IU/l, before making a judgement of unmet need for specialist investigation.

It is possible that additional previously undetected physical abnormalities might have been identified if we had included a detailed physical examination and additional investigations such as a chest X-ray and urinalysis. The high level of physical morbidity in this population of long-term psychiatric patients is consistent with the results of other surveys (Sturt *et al*, 1982), including a survey of a younger population of 329 acute psychiatric admissions, which found that 43% had positive laboratory or radiological findings or both (Glass *et al*, 1985), and a survey of 59 chronically mentally ill support programme users (Farmer, 1988), of whom 53% had undiagnosed medical problems and 36% problems requiring a change of management. To the best of our knowledge, the present survey is the first that also provides systematically identified estimates of the degree of *unmet* need for physical investigation and treatment in such a population. In our view this provides a much more useful guide for planners and providers of clinical services. These findings should be judged in the light of other reports on the Camberwell High Contact Survey, in which details of the psychiatric and social services and the background population characteristics are fully described (Brugha *et al*, 1988; Brewin *et al*, 1988).

The high proportion of long-term day service users with physical health problems that require medical care raises concerns that carry implications for resources. The cost of the clinical pathology screen was £76 per patient and the cost of the two most productive tests, namely, those of thyroid and liver function, was £25 per patient. The clinical and laboratory screens established the presence of an unmet need for nine general hospital out-patient clinic assessments (Table I, column 9). However, failure to detect liver and thyroid disorder could have led to hospital in-patient care costs per patient of approximately £300 per day. Our survey of long-term day care users is based on an inner-city area with a population, in 1981, of 125 749 (Office of Censuses and Population Surveys, 1981). If our estimates of physical problems can be applied to the total sample ($n = 145$), rates for clinically assessed and laboratory assessed problems were, respectively, 47 and 51 per 100 000 of the total population, and our conservative estimate of overall unmet need for care was 10 per 100 000. It is likely that a similar survey of other long-term high-contact users of hospital, nursing home and other sheltered residential psychiatric services would add considerably to these estimates of need.

Although we uncovered relatively few important unmet needs for care, we are concerned that so many patients refused a laboratory pathology screening procedure, and that those found to have abnormalities were more likely to be disinclined to comply with treatment plans. Thus, our main hypothesis was partly supported, in that unmet need was more likely in those whose compliance was low. Furthermore, medical need was equally likely to be found in users of non-hospital day services, and we are concerned that medical supervision at day centres is not comparable with that provided at day hospital facilities for such long-term patients.

In conclusion, in our view long-term mentally ill patients in the community require close medical supervision, and should be strongly encouraged to agree to regular checks on their physical health.

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A Profile of Long-Stay Psychogeriatric Patients

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An assessment of 106 long-stay psychogeriatric in-patients in an East London borough was made using the CAPE and supplementary items in order to obtain a comprehensive picture of their needs; 51 long-stay residents in the care of local authority social services provided a comparison. Patients in hospital were found to be more disturbed, more disabled and more dependent than residents in local authority care.

The care of long-stay psychogeriatric patients is commonly considered to be the 'Achilles' heel' of psychiatry of the elderly. The *International Journal of Geriatric Psychiatry* (1986) comments that, in Britain, although we can be proud of our community-based programmes for the elderly mentally ill, long-stay care in both hospitals and local authority homes is "rapidly becoming a national disgrace". It is characterised by deteriorating facilities, poor staff:patient ratios and inactive homes (*International Journal of Geriatric Psychiatry*, 1986) as well as potentially hazardous misplacements in long-stay wards and homes (Kidd, 1962; Smith & Lowther, 1976; Wilkin *et al*, 1978). The increase of the elderly population, coupled with economic constraints in both health and social services, increases the pressure upon provision for the elderly in care.

At present there is a paucity of literature detailing the true profile of long-stay psychogeriatric patients. This, combined with the fact that there is still no clearly agreed standard for the care of the elderly mentally ill (Mann *et al*, 1984*a*), impedes the planning of provisions necessary to improve or even understand the principles of long-stay care. It is clear that more detailed assessments are required.

A substantial contribution to the assessment of the elderly has been made by tests of "activities of daily living" (ADL tests) (Lyle, 1984), but these are limited in the range of skills they cover and are not appropriate for use with the very severely impaired dementia patient. Various other methods are currently available, however; these range from detailed descriptions of health and self-care behaviour to short analyses of behavioural deficiencies (Huppert & Tym, 1986; Woods & Britton, 1985). Many of these scales are unsuitable for large-sample surveys where a rating scale is required, but a few scales, similar in all but detail, have been published which warrant attention (Blessed, 1985).

The Stockton Geriatric Rating Scale (Meer & Baker, 1966) has been shortened and combined with a cognitive performance test to produce the Clifton Assessment Procedures for the Elderly (CAPE) (Pattie & Gilleard, 1979). The CAPE, "a well rounded ... deservedly popular instrument" (Woods & Britton, 1985), consists of a number of items about behaviour which are rated by observers on a scale of three points. Subscale scores can be derived for a number of categories of behaviour (e.g. social disturbance, physical disability) and the scale can be used to generate global 'dependency' grades. These grades range from A (independent) to E (maximum dependency) and they may be obtained for both the Behaviour Rating Scale and the Cognitive Assessment Scale of the CAPE. The fact that the CAPE is in common use in the UK and that it satisfies Hall's (1980) minimal criteria for acceptability for rating long-stay patients significantly influenced our choice of it for the present study.

Our study was aimed at the population of long-stay psychogeriatric patients currently resident in hospital in one London borough. We wanted to describe the patients' needs in detail in order to make an informed decision about the most appropriate placement for them. To this end, and following Weissman's (1975) suggestion that innovations should supplement intact, standard scales, a series of items were written to supplement the CAPE. The assessment of individual patients was further broadened to include a full medical assessment. In addition, and because there were data already available about levels of dependency in local authority community settings to show that residents could be expected to show similar levels of dependency (Pattie & Gilleard, 1979; McPherson *et al*, 1985), we were interested to assess the residents from one of the borough's more 'dependent' local authority homes. However, our clinical impressions were contrary to the view that residents in local authority homes would be as disabled as those in hospital.

Method

All patients from one London borough sleeping on long-stay psychogeriatric wards between January and March

1987 were included in the survey. Those who died before all the data had been collected, those who had been admitted during the last two weeks of the study, and those who had been admitted before the age of 65 (i.e. the 'graduates') were excluded. The 106 remaining patients were assessed using the CAPE and a series of supplementary items, and they were given a medical assessment. All 51 residents of one local authority long-stay home ('Part III home') were also assessed using the CAPE and its supplementary items. This home was chosen for comparison because it was known to take the more dependent and disabled clients. CAPE ratings for subjects in both groups were completed by the researcher, who also interviewed staff for their opinions; finally, medical assessments were completed for the in-patients and case-note data were collected for the residents in the Part III home.

Materials

To supplement the information provided by the CAPE, 26 items were selected on the basis of discussions with clinical and academic staff to cover physical state (e.g. eyesight, hearing, problem behaviour (shouting, aggression, self-harm etc.)) and social competence (interests, initiative, social skills). They were written as short statements accompanied by a defined three-point forced-choice response, the form thus being consistent with that of the CAPE items. The new items were assessed in a pilot survey of 20 patients rated by at least two staff each, and those items which appeared to replicate CAPE items (following factor analysis) or which yielded inter-rater agreement of less than 80% were discarded. Copies of the final items are available on request.

Results

There were no significant age or sex differences between the in-patients and the Part III residents. There were more women than men in both settings (ratio 2.8:1). Mean age was 80 years 2 months for the in-patients and 82 years for the residents; median length of stay was 25 months and 31 months respectively, with a range of 3 weeks to 15 years. Most (86%) of the in-patient sample were given a diagnosis of dementia, which was confirmed by the medical assessment. Data from case notes for the resident sample were not considered sufficiently up to date or reliable to be reported in detail, and it was decided to rely on the assessment of problem behaviour based on the CAPE and supplementary items as the better index of the challenge to carers.

TABLE I
Cognitive Assessment Scale grades

Grade	*In-patients*				*Part III residents*			
	Male (n=25)	*Female (n=81)*	*Total (n=106)*	*%*	*Male (n=14)*	*Female (n=37)*	*Total (n=51)*	*% (n=51)*
A	0	0	0	0	1	1	2	4
B	1	1	2	2	4	4	8	16
C	1	3	4	4	4	19	23	45
D	3	6	9	8	3	3	6	12
E–low score	7	34	41	39	1	4	5	10
E–untestable	11	30	41	39	0	2	2	4
E–total	18	64	82	77	1	6	7	14
Incomplete[1]	2	4	6	6	0	3	3	6
Refusal	0	3	3	3	1	1	2	4

[1] Blindness or other handicaps.

TABLE II
Behaviour Rating Scales grades

Grade	*In-patients*				*Part III residents*			
	Male (n=25)	*Female (n=81)*	*Total (n=106)*	*%*	*Male (n=14)*	*Female (n=37)*	*Total (n=51)*	*% (n=51)*
A	0	0	0	0	4	2	6	12
B	0	0	0	0	1	7	8	16
C	1	4	5	5	6	10	16	31
D	4	13	17	16	3	9	12	24
E	20	64	84	79	0	9	9	18

TABLE III
Association of BRS and CAS grades in long-stay psychogeriatric wards[1]

BRS \ CAS	A	B	C	D	E
A					
B			2 (2%)		
C			2 (2%)	1 (1%)	2 (2%)
D				4 (4%)	7 (7%)
E				11 (10%)	74 (61%)

1. CAS refusal = 3.

CAPE dependency grades

Overall dependency grades were established for in-patients and residents using the Behaviour Rating Scale (BRS) and Cognitive Assessment Scale (CAS) of the CAPE. Table I shows the distribution of dependency grades calculated on the basis of the CAS. The inpatients were found to have a significantly higher level of dependency than the residents ($\chi^2 = 65.8$, d.f. = 4, $P < 0.001$). The dependency grades obtained from the BRS (Table II) show a similar pattern ($\chi^2 = 72.9$, d.f. = 4, $P < 0.001$).

TABLE IV
Mean CAPE scores

	In-patients	*Part III residents*	*Chronic psychogeriatrics*[1]
BRS			
Physical disability	8.11	4.31	7
Apathy	7.84	7.04	8
Communication difficulties	1.95	0.80	1
Social disturbance	2.42	1.25	2
BRS score	20.75	11.92	19
s.d.	6.71	3.99	–
t	10.30*		
CAS			
Information/ orientation	1.23	5.38	2
Mental ability	1.82	6.90	3
Psychomotor	0.46	3.33	1
CAS score	3.28	16.00	6
s.d.	5.79	7.99	
t	−9.68*		

1. Mean scores for a sample of "chronic psychogeriatric" patients quoted by Pattie & Gilleard (1979), p. 17.
*$P < 0.001$.

TABLE V
Discriminant function–CAPE items[1]

BRS number	*Item*	*In-patients*			*Part III residents*	
		Mean score	*s.d.*	*%*[2]	*Mean score*	*s.d.*
6	Appearance is disorderly	1.85	0.45	96	0.76	0.93
3	Is incontinent of urine and/or faeces	1.58	0.75	85	0.51	0.78
8	Helps out in ward/home	1.84	0.51	94	1.59	0.75
14	Is objectionable during day	0.81	0.83	54	0.39	0.67
4	Is in bed during day	0.06	0.24	6	0.18	0.48
10	Socialises with others	1.39	0.76	83	0.35	0.67
11	Is willing to do things suggested	0.83	0.76	61	0.82	0.79
–	CAS grade (1 to 5)	4.90	1.13	NA	3.78	1.60
2	Walking	1.16	0.84	44	1.10	0.83
5	Is confused	1.46	0.73	86	0.66	0.77
12	Understands communication	0.85	0.79	61	0.18	0.48
16	Accuses others	0.26	0.55	21	0.16	0.46

Canonical correlation = 0.73, $\chi^2 = 121.18$,* known subjects correctly classified = 87.87%

1. All scores have a maximum value of 2 unless otherwise indicated.
2. Percentage of patients scoring 1 or 2 on these items.
*$P < 0.001$.

TABLE VI

Discriminant function – CAPE and new items[1]

	Item	In-patients		Part III residents		
		Mean score	*s.d.*	%[2]	*Mean score*	*s.d.*
(New)	Nurses' recommendation (1 to 7)[3]	6.61	1.15	NA	3.80	0.73
(BRS)	Appearance is disorderly	1.85	0.45	96	0.76	0.93
(New)	Steals	0.125	0.47	7	0.02	0.14
(BRS)	Is in bed during day	0.06	0.24	6	0.18	0.48
(BRS)	Helps out in ward/home	1.84	0.51	94	1.59	0.75
(New)	Doctor's recommendation (1 to 7)[3]	6.35	1.32	NA	4.40	0.99
(New)	Harms others	0.42	0.73	27	0.14	0.45
(New)	Accepts/rejects nursing assistance	0.78	0.76	59	0.34	0.66
(BRS)	Socialises with others	1.39	0.76	83	0.35	0.67

Canonical correlation = 0.85, $\chi^2 = 198.44$,* known subjects correctly classified = 92%

1. All scores have a maximum value of 2 unless otherwise indicated.
2. Percentage of patients scoring 1 or 2 on these items.
3. 1 – home without extra support; 2 – home with extra support; 3 – warden-supervised housing; 4 – old people's home; 5 – geriatric ward; 6 – hospice; 7 – psychogeriatric ward.

Table III illustrates the skew towards maximum dependency shown by the in-patient group: 74 patients (60.9%) scored E on both scales ('double E'), whereas this is true for fewer than 20% of the Part III residents.

As our interests in the present study were mainly directed towards delineating the particular needs of the individual patients, it was of special interest for us to look at the results of the subscales and the supplementary information. The mean scores on the subscales of the CAPE are shown in Table IV, and it can be seen that items relating to the level of physical handicap and to cognitive abilities show the largest differences between in-patients and residents.

The supplementary items which were developed on physical/medical state, problem behaviour and social competence further illustrate these differences, although in terms of overall group discrimination they added little to the predictive power of the CAPE dependency grade. Discriminant function analysis was employed to examine the discriminating power of the CAPE plus the new items in predicting the two categories of subject (in-patient and resident). Tables V and VI show the items which achieved significance.

It can be seen from these tables that the correct classification of subjects by the addition of the new items increases by a very small amount, from 87.87% to 92%. This is a statistically non-significant improvement, which nonetheless has clinical value in terms of the additional description which the items provide for individuals assessed on the scale.

Exceptionally high proportions of the in-patient sample were rated as follows: 86% as confused, 85% as incontinent, 96% as of disorderly appearance when left to their own devices, 83% as unable or unwilling to socialise, and 94% as unable or unwilling to help out on the ward. Moreover, 61% were rated as understanding very little of what was communicated. These characteristics made an elderly person in this study more likely to be found on a long-stay psychogeriatric ward.

Discussion

The present study has produced a profile of patients selected for long-stay care by a succession of psychogeriatricians in an East London borough. This profile should also provide a guide to most long-stay psychogeriatric patients 'hidden' in other long-stay psychogeriatric wards, and may also be useful for 'weeding out' patients in long-stay units who are not sufficiently incapacitated or disturbed to be there and should instead be in a residential home. To those of us in the borough who have been aware of the tendency for community residential facilities for the elderly to take increasingly dependent clients, the contrasts found in our study between the in-patient sample and those in the local authority home came as something of a shock. Our results nonetheless confirmed the clinical impressions of staff on the wards that they did contain the more disabled group of patients. Much recent interest has been shown in the disturbance and disabilities of Part III residents (Mann *et al*, 1984*b*), and our findings may stimulate new discussion. Most of the patients in the in-patient sample obtained a maximum dependency score; the mean scores for the CAPE subscales were typically 'worse' for our long-stay psychogeriatric in-patients than the scores published by Pattie & Gilleard (1970) for a "chronic psychogeriatric sample", and the range of types of problem behaviour identified was so extensive that it presented a clear challenge to both carers and planners alike. We are hopeful that the date will assist in the development of appropriate local plans for the provision of long-term care.

Other research has shown that the quality of the environments in which we care for elderly dependent people, the staffing and the organisational factors are central to the debate about the form that long-term care should take. These factors are frequently cited in the literature as influential in the development of 'the institutional syndrome'. As important, but often forgotten it seems, is a detailed exposition of the individual needs of the clients themselves. In this study we attempted just that and we found differences to characterise the elderly person in a long-stay psychogeriatric ward. While it is clear that organisational features, staff factors and physical environment can have a powerful effect on the frequency of disturbed or disruptive behaviour and on the engagement of vulnerable elderly clients (it is interesting to note that Apathy subscale scores - which one might suppose to be the more vulnerable to the effects of environmental influence - were disturbingly high for both client groups in our study), we did not investigate the relationship between these variables. We were primarily concerned to examine the needs of a population - the long-stay psychogeriatric in-patient population - which is under-represented in the literature and which must be adequately described if its needs for care in the long term are to be met. Having said this, however, we were made very aware of the importance of appropriate support for staff: for some, their own 'engagement' was perilously close to withdrawal, whereas others managed to persevere in the provision of high-quality nursing care despite the heavy odds. Even though we did not examine these factors in detail, it is clear that staff needs must be addressed in very clear terms in the provision of alternative long-stay settings.

Finally, we have no reason to suppose that the problems identified in the present study are so different from the problems which could be described in any other London borough. As a consequence, we find ourselves wondering about the appropriateness of general plans for provision in the community and for the closure of hospitals. The results of our own assessment led us to reconsider plans for the re-siting of some patients, and focus instead on the quality of the service provided in the one location. It is to be hoped that the results of our survey and the creation of new items to supplement the CAPE have given carers and planners a better platform to work from, and that we have provided a model for the assessment of individuals at a time when large-scale group surveys are the more usual course of action.

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Life Events, Life Difficulties and Confiding Relationships in the Depressed Elderly

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A total of 101 elderly depressed patients and 85 community residents (matched for age and sex) were interviewed about life events, difficulties, and confiding relationships. Significantly more of the depressed sample reported at least one severe event in the three months before the onset of their illness. Lack of a good confiding relationship was associated with depression in men but not in women. In this relatively affluent Australian sample, life difficulties were rare and, probably as a result, were not significantly associated with depression.

Research over many years has suggested that there is a strong association between stressful life events and the onset of depressive illness. Brown & Harris (1978) have argued that the association is in fact a causal link. They found that in 68% of onset cases of depression among adult women in the community, at least one severe life event was reported for the 38 weeks before onset, compared with 20% of normal women in a comparable period of time. Most of the difference in the reporting of life events occurred in the nine weeks before onset or interview.

Brown & Harris (1978) established these findings using the Bedford Life Events and Difficulties Schedule, a semistructured interview which varied considerably from the use of life event check-lists, the hallmark of previous approaches to such research. Furthermore, events were rated on a four-point severity scale, not by the respondent but by trained raters, who remained ignorant of the respondent's subjective view of any distress caused by the events. These ratings have been found to be reliable, including those made on events reported by the elderly (Wilkinson *et al*, 1986).

Post (1962) wrote that, in his experience, most depressive illnesses in elderly people appeared within a few days, weeks or months of some outstanding or incisive occurrence in their lives. He found a precipitating factor in 67 of his 100 patients, including 60 where there was an actual or threatened loss, either a loss of health (24), loss of sources of affection (20) or loss of objects (16).

Murphy investigated the association of life events with the onset (Murphy, 1982) and the outcome (Murphy, 1983) of depression in the elderly. She modified the Bedford interview for use with this age group, who experience crises different to those of younger people. She found that difficulties, especially those involving personal health, had a strong association with both the onset and the outcome of depression in the elderly. This is in contrast to the findings of Brown & Harris (1978), who reported that, in their younger sample, only those major difficulties which did not involve personal health were associated with an increased risk of onset of depression.

Vulnerability factors were defined by Brown & Harris (1978) as factors which were associated with a higher risk of depression if a severe life event had also occurred, but not otherwise. Of their four vulnerability factors in younger women, only the lack of a confidant was found by Murphy (1982) to play a role in depressive illness in the elderly. Murphy found that the early loss of a mother was not important, and the other two were not relevant in this age group.

The investigations of Brown & Harris were confined to women aged 18–65 years. Murphy studied people aged 65 years or older, but did not analyse her data by sex. Whereas Brown & Harris examined the relationship between depression and severe life events in several time periods during the months before the onset of depression, Murphy reported findings for the entire 12 months before onset only. Burvill *et al* (1989) have conducted a study of depressive illness in the elderly in Perth, Western Australia, which provided the opportunity to study the association between severe life events and difficulties and depression in the elderly, for each sex separately, and for each of four three-month periods before onset. Four hypotheses were tested: (a) that the proportion of individuals who report at least one severe life event in the year before onset will be higher among depressed elderly patients than in a normal community group; (b) that the difference between patients and controls will be greatest in the months closest to the onset of depression; (c) that there will be an excess of both social and personal health difficulties in the depressed group; and (d) that the depressed group will be more likely to report confidants as absent or poor.

Method

Two groups of subjects were interviewed. The first was a group of depressed elderly patients and the second a group of non-depressed elderly people selected from the general population. The depressed group comprised 101 patients drawn from three general hospitals, two mental hospitals and two psychogeriatric assessment centres: there were 85 in-patients being treated by psychiatrists, 9 geriatric in-patients about whom a psychiatrist was consulted, and 7 out-patients seen by psychiatrists. The community group comprised 85 people selected randomly from the electoral roll of residents of private dwellings in two Perth (Western Australia) districts, and then matched with the depressed group for age and sex.

Inclusion criteria and interview

People were included if they were 60 years of age or older and were able to speak sufficient English both to understand and to participate in the study. The depressed group was required to fulfil the DSM–III (American Psychiatric Association, 1980) criteria for major depression and to have been depressed for at least four weeks. The primary diagnosis had to be depression, not dementia. Patients were deliberately not excluded if they showed signs of cognitive impairment, since cognitive impairment is said to be an important prognostic factor for the outcome of depression and we wished to test this in a later part of the study. However, those who were included were not severely cognitively impaired (Mini Mental State Examination scores ranging from 18 to 23). Thus it seemed unlikely that the validity of their answers in the interview was threatened by their being significantly demented. The community group were given the 30-item General Health Questionnaire (GHQ; Goldberg, 1972). Only those who scored 4 or less were included in the study to minimise the probability of mental illness in this group.

Two interviews were conducted. The first was a psychiatric interview conducted by a psychiatrist or third-year psychiatric registrar, to ensure that all patients met the diagnostic criteria. An important detail ascertained during this interview was the date of onset of the patient's index illness of depression. This was dated as precisely as possible in order to define the 12-month period prior to onset. If the interviewer was not certain about the date of onset then it was clarified by the clinical notes being read and the patient's relatives being asked. It was possible in all cases to define a time when the patients first showed definite symptoms of their illness.

The second interview, which collected social and psychological data, was conducted by a psychology graduate and trained nurse (JE). It included the demographic questionnaire, the Interview Schedule for Social Interaction (ISSI; Henderson *et al*, 1981), the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975), and the Bedford Life Events and Difficulties Schedule (Brown & Harris, 1978) modified for the elderly (Murphy, 1982).

When using the modified Bedford interview, the interviewer was instructed to ask the person about the existence and quality of his or her confiding relationships. The Interview Schedule for Social Interaction also assisted the researcher to classify the person's confidants. The guidelines suggested by Brown & Harris (1978) and used by Murphy (1982) were collapsed to form two categories of confidant: 'good', which included intimate relationships with the spouse or with a friend of either sex who was seen on a regular basis and could be relied on to give advice; and 'poor or none', which included conflicted relationships with a spouse, a spasmodic relationship or no one to confide in at all.

The community residents were sent an introductory letter to explain the study, giving them an opportunity to contact the research team if they had any enquiries. Within two weeks of the letter being sent, the interviewer followed it up with a visit. If no answer was obtained, up to four visits to the house were made. The response of the community residents was excellent, with only 8 out of 97 people refusing to take part. Four others were omitted from the study because their scores on the 30-item GHQ were 5 or above. The demographic data of these four respondents did not differ in any way from those of the remainder of the group. The interview consisted of the same schedules as for the depressed sample, with the 12 months before interview being the time period defined when using the Bedford interview.

All life events and difficulties reported by the depressed and community respondents were rated by three of the authors (JE, PWB, and RF-J), one of whom (RF-J) had been trained in Brown's unit. JE was the only one of the three raters who knew if the events discussed had been reported by a depressed or community respondent. All life events were assigned a rating on a four-point severity scale developed by Brown & Harris (1978), with the aid of their life event dictionary. All events were also given a focus rating, depending on whether the events had happened to the respondent or to some other person. In the occasional case, if the event was not listed in the dictionary, it was summarised and sent to T. Harris who made comments on the rating given. In all of these cases the rating made by T. Harris was the same as that of the rating panel. In this way we made every effort to use criteria comparable to those used by Brown & Harris (1978).

Life difficulties were defined by the criteria of Brown & Harris (1978) and were also rated for severity at the consensus meetings. This rating was on a six-point scale, which was later collapsed into severe and non-severe difficulties. By definition, life difficulties were ongoing problems from which the subject had suffered for at least six months. For example, a cerebral vascular accident eight months ago would have constituted an event, but any subsequent health or mobility problems which may have resulted from the accident would constitute a life difficulty.

Data analysis

The central focus of this investigation was whether the frequency of severe life events or difficulties differed between the elderly depressed patients and the community residents, and whether this relationship was modified by age and sex, and the presence or absence of a confiding relationship. These questions were addressed by testing the fit of log-linear models (Hall & Bird, 1986) to the contingency tables produced when group membership (depressed or community sample) was cross-classified by age, sex, confidant status, and occurrence of life events and difficulties.

The fit of different log-linear models was assessed by the stepdown deletion of higher order interaction terms using the SYSTAT package (Wilkinson, 1986). For example, in testing whether relationships between life events and depression were affected by age, we first tested the fit of the model which included all main effects (age, life events, group membership) and all two-way interaction effects, but which omitted the three-way interaction between these variables. If this model fitted the data, this would indicate that there was no need to include a three-way interaction term in the model. If the three-way term could be omitted, a similar process would be carried out to decide which if any of the two-way interaction terms could be deleted from the model.

Results

Log-linear analyses showed that the reporting of a severe life event in the three months before onset was significantly associated with depressed group membership, and that this remained true when all other factors were included in the analyses. Second, lack of a good confidant was significantly associated with depression for men only. This was so even after severe life events were included, and (for men) the association seemed even stronger than that of a severe life event. Third, age, sex and life difficulties were not associated with depressed group membership. These results are presented in more detail below. The age and sex distribution of the 101 depressed patients and 85 community residents is given in Table I.

TABLE I
Age and sex distribution of the depressed and community samples

	Age 60–69 years	*Age 70–79 years*	*Age 80+ years*	*Total*
Depressed sample				
Men	14	14	9	37
Women	26	28	10	64
Community sample				
Men	10	13	7	30
Women	21	26	8	55

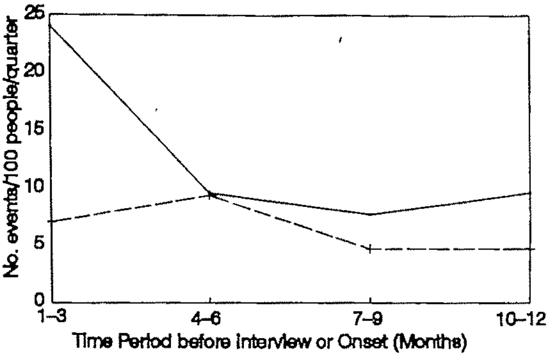

FIG. 1 Severe life events per 100 people per quarter year, for depressed (——) and community (---) samples.

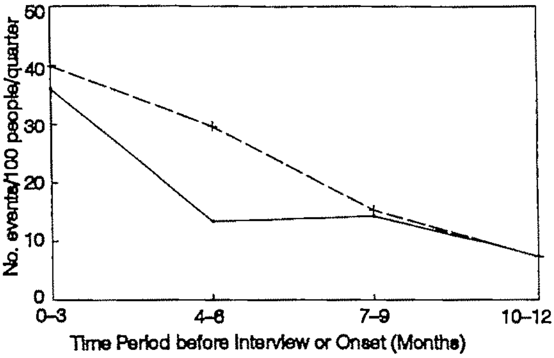

FIG. 2 Non-severe life events per 100 people per quarter year, for depressed (——) and community (---) samples.

Life events

The rate of life events per 100 people per three-month period among the depressed patients and the community residents was calculated for severe and non-severe events separately (Figs 1 and 2). The raised rate of severe life events among the depressed patients in the three months before onset was not due to a high number being reported by just a few patients: 24% of the depressed patients as compared with 7% of the community group reported at least one severe event in the three months before onset or interview ($\chi^2 = 10.21$, d.f. = 1, $P < 0.01$). For the full year the corresponding percentages were 38% and 19% ($\chi^2 = 8.12$, d.f. = 1, $P < 0.01$). It can be seen that the 12-month difference between the depressed patients and the community residents was due to those events occurring in the three months before onset, since similar proportions (14% of the patients and 12% of the community residents) reported a severe event in the remaining nine months.

The difference between the patient and community groups was not due to 'illness' or 'hospital admission' events in the patients. In all cases, the onset of depression preceded these events, which were consequently excluded. Log-linear analyses showed no significant interactions when we examined the effects of age and sex on the relationship between life events and group membership. In other words, the difference between patients and residents held for both sexes and did not vary with increasing age over 65 years.

The link between severe life events and depression did not vary when two indices of the severity of depression were specified. These were the DSM-III categories of major depression, major depression with melancholia, and major depression with psychosis, and three categories based on Hamilton Rating Scale for Depression scores of <20, 20–29, and >29. We found that the association with severe life events was the same for endogenous and neurotic depression, as measured by the Newcastle scale (Carney *et al*, 1965).

The numbers of respondents reporting at least one non-severe life event were not significantly different in the depressed group (49, or 48%) and the community group (44, or 52%).

Table II shows the rate of reporting of different types of event by the depressed and community groups. There were two important findings. First, if the rates of severe and non-severe events are combined, there is no difference between the depressed group and the community group. The two groups differ only for severe events. Secondly, the difference is mainly due to deaths and to illnesses rated as severe. 'Other' events were made up of various categories such as holidays, births, marriages, separations and retirements, and ratings of 'severe' were rare for such events.

TABLE II

Number of events reported per 100 people in the three months before onset or interview

	Severe events		*Non-severe events*	
	Depressed	*Community*	*Depressed*	*Community*
Death	7	2	4	7
Illness	16	5	17	24
Other	3	0	16	10
Total	26	7	37	41

TABLE III

Distribution of depressed and community samples by sex, life event and relationship status

	Life event and relationship status		*Depressed*		*Community*	
	Severe event	*Poor/no confidant*	*No.*	*%*	*No.*	*%*
Men	Yes	Yes	6	16	0	0
	Yes	No	4	11	3	10
	No	Yes	15	41	1	3
	No	No	12	32	26	87
Total men	—	—	37	100	30	100
Women	Yes	Yes	3	5	1	2
	Yes	No	11	17	2	4
	No	Yes	11	17	9	16
	No	No	39	61	43	78
Total women	—	—	64	100	55	100

Life difficulties

The number of subjects who reported a severe life difficulty was surprisingly low, being 15% of the depressed sample and 7% of the community sample, and the difference was not significant. There was no difference between the groups in the number of non-severe life difficulties, with 11% of the depressed group and 13% of the community group reporting one. No person reported more than one life difficulty. The types of difficulty experienced by the subjects were nearly all personal health difficulties: 11% of the depressed and 7% of the community sample reported severe health difficulties. The remaining 4% of depressed patients reported a social difficulty.

Confiding relationships

There were significantly more depressed patients with a poor or no confiding relationship (35/101 in the depressed group compared with 11/85 in the community group, $\chi^2 = 12.24$, d.f. = 1, $P < 0.01$). Log-linear analysis showed a significant interaction between sex and confidant on group membership. This was because the confidant difference was restricted to men, with 57% of depressed men and 3% of community men reporting a poor or no confidant. The corresponding figures for women were 23% and 18% (Table III). We wondered if depressed men were more likely to rate a confidant pessimistically as poor, so we repeated the analysis, this time comparing only those with and without any confidant at all, and removing those who described themselves as having a poor confidant. The interesting sex difference persisted. We found that 45% of depressed men and 3% of community men reported having no confidant at all, while the corresponding figures for women were 6% and 4%.

Further log-linear analyses were performed using the data for men only. Not surprisingly, these showed a significant two-way interaction between the type of confiding relationship and whether the subject was from the depressed or community group ($\chi^2 = 24.47$, d.f. = 2, $P < 0.001$). The odds of depressed men having poor or no confiding relationships were 21:16, while those for male community residents were 1:29, producing an odds ratio of 38:1. In contrast, for the reporting of a severe life event, the corresponding odds ratio for depressed male patients versus male community residents was only 3:1 (see Table III for the raw data).

Discussion

Burvill *et al* (1989) have discussed the representativeness of the depressed sample reported here. They concluded that the sample was representative of severely depressed patients treated by Perth psychiatrists. The community sample was selected randomly from the electoral roll and was then matched with the depressed group for age and sex.

One major issue when using interview data from an elderly group is unreliability due to problems associated with forgetting. Murphy (1982) conducted a small reliability study using next of kin to confirm the information given by elderly patients and found that information could be collected with reasonable accuracy. Ridley *et al* (1979) studied recall in elderly women and found that they could remember accurately major life events in their lives. This was consistent with our findings, in that the rate of reporting of severe life events by depressed patients and community residents remained constant over 12 months, apart from the raised rate among the depressed patients in the three months before onset.

The results supported the first hypothesis tested in this study, namely that the proportion of individuals reporting at least one severe life event in the 12 months before onset would be higher in a depressed sample than in a community sample. As argued by Brown & Harris (1978), these events may have played an aetiological role in the illness, since they occurred before the onset of symptoms and were therefore independent of the illness. Although our results were broadly in keeping with the findings of Brown & Harris (1978) for younger depressives and Murphy (1982) for the elderly, the proportion of patients reporting a severe event in this study (38%) was lower than those found by Brown & Harris in Camberwell (61%) and Murphy in the East End of London (48%). We interpret these figures to mean that elderly depressed patients are less likely to report a severe life event (38%, 48%) than young depressed patients (61%). We do not believe the difference is due to area differences in the frequency of severe life events, since the proportions of normal community residents reporting a severe life event were much the same in Perth (19% in 12 months), Camberwell (20% in 9 months) and the East End of London (23% in 12 months).

The second hypothesis was upheld. When four consecutive three-month periods before onset were examined, the proportion of individuals reporting a severe life event was significantly greater among depressed patients than among community residents for one time period only, namely the three months immediately before onset. This was similar to the findings of Brown & Harris (1978), although, as for the 12-month figures, the proportion of patients reporting a severe event in three months was lower in our study (24%) than in the Camberwell study of younger female patients (42%). The corresponding figure for normal community residents in Perth (7% in three months) was similar to that in Camberwell (7% in nine weeks), making unlikely an explanation based on area differences in the frequency of life events. A similar comparison with elderly depressed patients in the East End was not possible because Murphy confined her analysis to the 12 months before onset.

There was little support in this study for the third hypothesis, that severe difficulties contribute to the onset of depression in the elderly. In our study, twice as many depressed patients as community residents reported a severe difficulty (15% v. 7%), but this was not a significant difference. Overall, very few difficulties were reported and they added nothing once severe events were taken into account. This is in contrast to the findings of Brown & Harris (1978), who reported that 47% of patients and 49% of onset cases had a major difficulty, as compared with 17% in their non-depressed community group. Similarly, Murphy (1982) found that 42% of patients had a major difficulty in the two years before onset, as compared with 19% of normal people. It is striking that no person interviewed in the Perth community reported a major social difficulty. One explanation for this is the high proportion of the elderly in Perth who are housed in hostel and nursing home facilities (the largest percentage in Australia). These people, who will not be found in a survey of those living in private dwellings, are by definition most likely to have endured a major social difficulty. Their absence from the sample might also explain the low prevalence of health difficulties. Another explanation is that, compared with both Camberwell and the East End of London, Perth is a much more affluent community, with less probability of elderly residents having severe social difficulties with housing and finances. That is, the elderly residents in Perth and the poorer parts of London are just as likely to be exposed to a severe life event, but have a different likelihood of encountering major social and health difficulties.

Murphy (1982) found that having no confidant at all was associated with an increased risk of depression, but only in the presence of a severe life event. Thus the absence of a confidant acted as a vulnerability factor as defined by Brown & Harris (1978). On the other hand, Henderson *et al* (1986) found that the depressed elderly living in the community did not report a lack of close relationships (although they did for more diffuse relationships), and speculated that their measure of intimacy measured something different from that of Brown & Harris (and hence Murphy). We provide yet a third result: we found that there was no difference between the depressed and community women in the number reporting poor or no confiding relationships, the majority having good confidants. The significant difference between the depressed and community group was accounted for entirely by the men, with almost two-thirds of the depressed men reporting a poor or no confiding relationship. Furthermore, this factor seemed to be associated with depression requiring admission in men even more strongly than were severe life events, judging by the odds ratios for the two. Without a sample of identified cases of depression in the community, we cannot say whether this impairment of relationships acts as a vulnerability factor or as a provoking agent of depression. It may be neither, acting merely as an influence on admission and not on depression.

We know that the sex difference we found in the link between depression and social relationships was not due to a sex-related difference in judging what a 'poor' confidant was, since the finding persisted when only those reporting no confidant at all were analysed. Repeating the analysis in this way also allowed us to compare our results with those of Murphy, revealing a possibly important area difference. Murphy found that 39% of the depressed patients and 18% of the community residents in London reported having no confidant at all, while the corresponding figures in Perth (ignoring the difference between men and women) were much lower, being 20% and 5%. We have no explanation for this area difference or for the sex difference in the association between depression and social relationships, and no help is afforded by the studies of Brown & Harris (1978), who examined only younger women, or Murphy (1982), who did not differentiate between the sexes. A possible interpretation is that depression results in a (distorted) judgement that one has a poor or no confidant. We are then left with explaining why this was true of men but not women, which we cannot do. Our results emphasise the desirability of examining further the role of confidants in both younger and older depressed patients, and differentiating between men and women.

Overall, this study has confirmed the association in the elderly between severe life events and the onset of depression requiring hospital admission, and thus partially replicates the results of Murphy (1982). Furthermore, we have shown that this association is due to severe life events occurring only in the three months immediately prior to the onset of depression, just as it is in the younger women reported by Brown & Harris. We found that enduring life difficulties were not common in this particular sample of the elderly, and, perhaps as a consequence, were not important in the onset of depression. Finally, we detected a significant sex difference in the link between social relationships and depression requiring admission. Our inability to explain this result satisfactorily underlines the importance of detecting cases of psychiatric disorder at both the hospital and community level when studying the role of social factors in their onset, and of differentiating between men and women.

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Impaired Lymphocyte Stimulation by Mitogens in Severely Depressed Patients
A Complex Interface with HPA-axis Hyperfunction, Noradrenergic Activity and the Ageing Process

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To investigate the relationships between the immune apparatus, major depression, and HPA-axis and noradrenergic activity, the authors measured the lymphocyte stimulation responses to the mitogens phytohaemagglutinin (PHA), pokeweed mitogen (PWM) and concanavalin A (CON A), post-dexamethasone cortisol (DST) values and 3-methoxy-4-hydroxyphenylglycol (MHPG) excretion in 24-hour urine samples from 48 patients. We found that lymphocyte responses to PHA and PWM in melancholic and psychotic depressives were significantly lower than in minor depressives. The lymphocyte responses to PHA, PWM and CON A showed significantly negative correlations with age, DST results and HRSD score. Responses to PHA were significantly negatively correlated with MHPG excretion. Up to ±33% of the variance in the three mitogenic lymphocyte responses could be explained by canonical correlation with age, DST results and MHPG values.

The last decade has produced a series of studies which indicate that severe depression can endanger the immunological function (Calabrese *et al*, 1987). Lymphocyte stimulation responses to the mitogens phytohaemagglutinin (PHA), concanavalin A (CON A) and pokeweed mitogen (PWM) are immune parameters which were found to be impaired in major depressives (Schleifer *et al*, 1984, 1985; Kronfol & House, 1985; Kronfol *et al*, 1986). The stimulation of lymphocytes by PHA, CON A and PWM is an *in vitro* technique used to assess the functional capacity of T (PHA, CON A, PWM) and B (PWM) cells, i.e. it is a correlate of cell-mediated immunity (Roitt *et al*, 1985). A conventional method of evaluating this responsiveness to mitogens is measuring ^{3}H thymidine incorporation after culturing the lymphocytes in the presence of concentrations of between 0.4 and 200 μg/ml of PHA, CON A and PWM.

Recently, it has been shown that there is an integrative level of regulation of immune competence mediated by neuroendocrine and autonomic signals (Calabrese *et al*, 1987). Neuroendocrine-immunomodulation is mediated in part by the hypothalamus and the pituitary gland (Brooks *et al*, 1982; Cross *et al*, 1982). Glucocorticoids exert a profound immunosuppression through several mechanisms (Calabrese *et al*, 1987). Catecholaminergic 'spillover' during sympathetic activity may also affect immunocompetence (Calabrese *et al*, 1987). Furthermore, there are data to support the novel concept that the immune apparatus may affect brain and adrenal function. The immune systems produce peptides which can stimulate cortisol secretion (McGillis *et al*, 1985). Products released from activated immune cells may induce decreased noradrenergic turnover in brain structures (Besodovsky *et al*, 1983).

Corticosteroid 'overdrive', as evidenced by disturbances in the dexamethasone suppression test (DST), is one of the most consistently reported abnormal findings in severe depression (Carroll, 1980; Feinberg & Carroll, 1984; Maes *et al*, 1986*a*). Noradrenergic hyperactivity is another characteristic of major depression (Maas *et al*, 1987; de Villiers *et al*, 1987; Maes *et al*, 1989). Also, excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG) (the major metabolite of noradrenaline) in 24 h urine samples has been shown to be altered during severe depression (Maes *et al*, 1987; Garfinkel *et al*, 1979).

Age is another confounding variable which could negatively affect lymphocyte stimulation by lectins (Kishimoto *et al*, 1978). The DST results (Oxenkrug *et al*, 1984; Alexopoulos *et al*, 1984; Lewis *et al*, 1984), plasma noradrenaline levels (Pfeifer *et al*, 1983) and MHPG excretion (Maes *et al*, 1986*b*) increase with age.

This prospective study has been undertaken in a group of depressive patients to investigate (a) if severe depressions are linked with an impaired immune competence as measured by PHA-, PWM- or CON A-induced lymphocyte stimulation, and (b) if there exist significant negative relationships between immunological responses and the DST results, MHPG excretion and age.

Method

Patients

The patients were 48 depressives consecutively admitted to the St Jozef Psychiatric Centre, Munsterbilzen, Belgium, from 1 May 1987 to 30 May 1988. The patients were categorised according to DSM-III (American Psychiatric Association, 1980) in the following groups: minor depression (Williams & Spitzer, 1982), including dysthymic disorder (300.40) and adjustment disorder with depressed mood (309.00); major depression without melancholia (296.X2); and major depression with melancholia and/or with psychotic features (296.X3, 296.X4). Diagnoses were made using the Structured Clinical Interview for DSM-III, Patient Version (Spitzer *et al*, 1985). The Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) score was measured five to seven days after the admission of patients into hospital. Bipolar patients, patients with substance use disorders and patients who had taken lithium, MAOIs and/or neuroleptics in the six months before admission were not included in this study.

Twenty patients were drug-free for at least one month before admission. The others had taken benzodiazepines and/or antidepressants. After admission, 26 depressives did not receive any medication at all. The others were on lorazepam ($\leqslant$6 mg/day) for agitation, anxiety or sleep disorders.

The subjects were free of chronic medical disorders associated with alterations in immunity. Patients who had a recent (<2 weeks) history of infectious disease were omitted. Furthermore, medical and laboratory tests (blood analysis, liver and kidney function tests, sedimentation rate, leucocytes and urine) showed no major pathologies. Carroll's (1980) exclusion criteria were applied to avoid false positive and false negative test results in the DST. Consequently, patients with a body weight less than 80% of ideal weight (calculated from wrist circumference and height) were excluded from the study.

Procedure

Eight days after admission of the patients into hospital, blood was sampled for the lymphocyte transformation tests at 8.00 a.m. after an overnight fast. At 11.00 p.m., 1 mg dexamethasone was administered orally. The next day, blood samples were taken at 8.00 a.m. for the determination of cortisol. Five days after admission into hospital, a baseline 24 h urine collection started at 10.00 p.m. From admission, patients were on a VMA-free diet. During the 24 h collection they were kept in a state of rest. The urine collection was considered complete if the creatinine excretion was more than 0.7 g/day and the urine volume more than 0.7 l/day (complete in 43 cases). Lymphocyte transformation tests were performed according to the technique described by Keller *et al* (1981). Peripheral blood lymphocytes were isolated from 15 ml heparinised venous blood by centrifugation over a Ficoll Hypaque gradient. Blood mononuclear cells separated by the Ficoll Hypaque method were cultured at 2×10^5 cells per millilitre in 0.2 ml triplicate aliquots in RPMI 1640 with 15% autologous serum for 3 days at 37°C in a 5% CO_2 atmosphere. Phytohaemagglutinin (PHA, Sigma L-4138), pokeweed mitogen (PWM, Sigma L-9379), and concanavalin A (CON A, Sigma C-5275) were added in 20 μl amounts to the microcultures to yield the following final concentrations: PHA 0.4, 2, 10, 50 μg/ml, CON A 5, 50, 100, 200 μg/ml, and PWM 0.4, 2, 10, 50 μg/ml. In control cultures, lectins were substituted by 20 μl of culture medium. After 72 hours, mitogenic activity was measured by adding 1 μCi of ^{3}H-thymidine (Amersham TRK 120, specific activity 25 Ci/mmol) and harvesting the cells 6 hours later. The ^{3}H-thymidine uptake was determined by β-counting. The means of triplicate determinations were calculated for each lectin concentration. The results were expressed as the difference of the counts per minute obtained for the lectin-stimulated cultures and for the unstimulated controls. The data (in counts/min) obtained after stimulation at the four final concentrations were added up and their sum was used in the statistical analyses.

TABLE I
Demographic data for the 48 depressed patients studied

Diagnostic categories	*Index*	*Ratio men/ women*	*Age*		*HRSD*	*Drug state*	
			Mean (±s.d.)	*Range*	*Mean (±s.d.)*	*BZ*[1] *yes/no*	*DF*[2] *yes/no*
Minor depression (300.40, 309.00)	md	8/11	39.5 (±16.6)	20–75	15.2 (±1.9)	9/10	8/11
Major depression without melancholia (296.X2)	MD−M	7/11	42.6 (±11.9)	28–67	20.3 (±2.7)[3]	8/10	8/10
Major depression with melancholia and/or with psychotic features (296.X3, 296.X4)	MD+M	4/7	47.1 (±12.0)	28–63	27.5 (±3.6)[4]	5/6	4/7

1. Use of benzodiazepines the day prior to blood sampling.
2. Drug-free period before admission to hospital: yes – more than 1 month drug-free; no – not drug-free.
3. Significantly different from md.
4. Significantly different from md and MD−M: all ANOVA, $F=74.73$, $P<10^{-5}$, d.f. = 2/47.

The cortisol assay was performed with a commercial enzymoimmunoassay kit (Eurogenetics, NMS Pharmaceuticals, New Port Beach, California). The inter-assay coefficient of variation (CV) was 9.5% ($\bar{X}=7.0\ \mu$g/dl, $n=32$).

MHPG in urine was determined by high-performance liquid chromatography, according to a procedure proposed by Moleman & Borstrok (1982) and slightly modified by Maes *et al* (1986*b*). In our laboratory the method yielded a CV of 9% ($\bar{X}=1$ mg/l, $n=10$). Creatinine in urine was determined using a kinetic Jaffé method (Claes, 1969).

Statistics

Relationships between variables were analysed by means of Pearson's product moment, the point biserial correlation calculation, multiple regression and canonical correlation analysis. For testing the group mean differences, the one-way analysis of variance (ANOVA), the factorial ANOVA, and the analysis of covariance (ANCOVA) were used. Multiple comparisons among treatment means were investigated with Fisher's least significant difference (LSD). The independence of classification systems was checked by means of the χ^2-test. Each measure was tested for normality of distribution by means of the Kolmogorov-Smirnov test. If the results were not normally distributed, transformations were used to reach normality of distribution. The significance was set at $\alpha=0.05$ (two-tailed).

Results

The demographic data for the 48 patients studied are shown in Table I. There were no significant differences either in the sex ratio or in age between the DSM-III categories. The HRSD scores were significantly different, increasing from minor depression to simple major depression to major depression with associated features. There were no significant differences in the drug state (use of benzodiazepines the day prior to blood sampling or the length of the drug-free period before admission) between the diagnostic groups.

The lymphocyte responses to PHA, PWM and CON A were normally distributed. The post-dexamethasone cortisol values approached the Gaussian distribution after logarithmic transformation. There were no significant effects of sex on the lectin-induced lymphocyte responses (results of factorial ANOVAs with sex as second factor). We found no significant biserial correlations between drug state and the biological variables (PHA, PWM, CON A results, DST and MHPG values) and the HRSD score. Major effects of drug state on our results thus could be disregarded.

The lymphocyte responses to the four different concentrations of PHA ($0.48 \leqslant r \leqslant 0.85$), PWM ($0.56 \leqslant r \leqslant 0.94$) and CON A ($0.53 \leqslant r \leqslant 0.90$) were significantly ($P<0.01$) intercorrelated. Also, the pooled data for the four concentrations of the three stimulants showed highly significant intercorrelations ($r>0.70$, $P<0.001$).

TABLE II

Mean (±s.d.) lymphocyte responses (ct/min × 10^{-3}) to PHA, PWM and CON A for the four concentrations of each stimulant

Index	*PHA*				*PWM*				*CON A*			
	50 µg/ml	*10 µg/ml*	*2 µg/ml*	*0.4 µg/ml*	*50 µg/ml*	*10 µg/ml*	*2 µg/ml*	*0.4 µg/ml*	*200 µg/ml*	*100 µg/ml*	*50 µg/ml*	*5 µg/ml*
md	71 (±60)	85 (±54)	43 (±29)	13 (±16)	24 (±16)	32 (±20)	48 (±35)	47 (±26)	51 (±32)	56 (±43)	54 (±44)	32 (±26)
MD−M	43 (±40)	58 (±39)	35 (±23)	8 (±12)	24 (±15)	32 (±19)	38 (±19)	42 (±18)	40 (±32)	35 (±26)	32 (±18)	25 (±21)
MD+M	28 (±25)[1]	43 (±43)[2]	29 (±33)	4 (±7)	13 (±11)	18 (±14)	20 (±12)[3]	25 (±14)[4]	28 (±23)	35 (±27)	32 (±18)	19 (±8)

1,2: Significantly different from md, ANOVA, d.f. = 2/47: $F_1=3.4$, $P=0.03$; $F_2=3.3$, $P=0.04$.
3,4. Significantly different from md and MD−M, ANOVA, d.f. = 2/47: $F_3=4.3$, $P=0.02$; $F_4=4.1$, $P=0.02$.

Table III

Mean (±s.d.) lymphocyte responses to PHA, PWM and CON A, post-dexamethasone cortisol values and MHPG in 24 h urine samples from the depressed patients

Index	*Lymphocyte responses (counts/min×10^{-3})*[1]			*Cortisol after DST (μg/dl)*	*MHPG (mg per 24 h urine)*
	PHA	*PMW*	*CON A*		
md	212 (±141)	150 (±78)	193 (±136)	2.04 (±2.47)	1.45 (±0.59)
MD−M	143 (±96)	135 (±66)	132 (±76)	2.86 (±4.03)	1.63 (±0.77)
MD+M	103 (±100)[2]	76 (±48)[3]	113 (±71)	7.63 (±6.21)[4]	1.56 (±0.67)

1. Pooled data for the four concentrations of the stimulants.
2. Significantly different from md, ANOVA, $F=3.36$, d.f. $=2/47$, $P=0.04$.
3. Significantly different from md and MD−M, ANOVA, $F=4.31$, d.f. $=2/47$, $P=0.01$.
4. Significantly different from md and MD−M, ANOVA on logarithmic transformations, $F=6.83$, d.f. $=2/47$, $P=0.003$.

Table IV

Differences in lymphocyte responses to mitogens between cortisol suppressors and non-suppressors

DST results	*Ratio men/women*	*Lymphocyte responses (counts/min×10^{-3})*		
		PHA	*PWM*	*CON A*
Non-suppressors[1]	8/6	98 (±76)[2]	86 (±52)[3]	98 (±55)[4]
Suppressors	11/23	188 (±129)	145 (±74)	174 (±115)

1. DST non-suppression is defined as post-dexamethasone cortisol values at 8.00 a.m. ⩾3.5 μg/dl.

2,3,4. Significantly different from suppressors, all ANOVA, d.f. = 1/47: $F_2=5.80$, $P=0.02$; $F_3=7.34$, $P=0.009$; $F_4=5.37$, $P=0.02$.

Lymphocyte responses and the DSM-III groups

Table II shows the measurements of the lymphocyte responses to PHA, PWM and CON A for the four concentrations used. Patients with major depression with melancholia and/or with associated features showed significantly lower lymphocyte responses to PHA than minor depressives (at the 50 μg/ml and 10 μg/ml concentrations). Major depressives with associated features exhibited significantly lower lymphocyte responses to PWM than minor and simple major depressives (at the 2 μg/ml and 0.4 μg/ml concentrations). No significant differences between the DSM-III groups were found in the CON A responses.

Table III shows the average values from the pooled data for the four concentrations of the three stimulants, the mean post-dexamethasone cortisol values at 8.00 a.m. and the MHPG values in the three DSM-III categories. Patients with major depression with melancholic and/or psychotic features showed significantly lower lymphocyte responses to PHA than minor depressives. They also showed a significantly lower PWM response than minor and simple major depressives. There were no significant differences in CON A responses between the diagnostic groups, although these responses tended to be lower in major depressives with associated features ($F=2.66$, d.f. $=2/47$, $P=0.07$). The pooled data for the four concentrations of PHA ($r=-0.29$), PWM ($r=-0.28$) and CON A ($r=-0.27$) were significantly ($P<0.05$) correlated with the HRSD score.

We found that major depressives with associated features had significantly higher post-dexamethasone cortisol values than minor and simple major depressives. We found no significant differences in MHPG excretion between the DSM-III groups (by means of ANCOVA, with creatinine and 24 h urinary output as covariates; see Maes *et al* (1986*b*)).

Relationships with DST results, age and MHPG excretion

Table IV shows the average values from the pooled data for the four concentrations of PHA, PWM and CON A for DST suppressors and non-suppressors (cortisol at 8.00 a.m. ⩾3.5 μg/dl (Maes *et al*, 1986*a*)). DST non-suppressors showed significantly lower PHA, PWM and CON A responses than DST suppressors. These differences remained significant even after introducing age as a covariate in an ANCOVA.

The pooled data for the four concentrations of PHA ($r=-0.38$), PWM ($r=-0.41$) and CON A ($r=-0.35$) were significantly ($P<0.01$) correlated with the DST results. Also, age correlated significantly ($P<0.01$) and negatively with these pooled data for PHA ($r=-0.45$), PWM ($r=-0.41$) and CON A ($r=-0.47$). The DST results and age were inversely correlated with all lymphocyte responses to the four different concentrations of PHA, PWM and CON A. All differences in PHA and PWM responses between the DSM-III groups disappeared after controlling for the DST results and age (results of ANCOVAs with DST results and age as covariates).

We found that the pooled data for PHA were inversely related to the adjusted MHPG data ($r=-0.30$, $P<0.05$).

MHPG excretion correlated negatively with the lymphocyte responses to PHA at 50, 10 and 2 μg/ml. A canonical correlation analysis was computed between the responses to the three mitogens (the first subset) and the DST results, age, MHPG, HRSD and drug state (BZ, DF) (the second subset). One canonical correlation ($r = 0.62$) was derived. Examination of the loadings of the individual variables showed that the canonical relationship was between PHA, PWM and CON A responses in the first subset (loadings 0.947, 0.883 and 0.925 respectively) and DST results, age and MHPG in the second subset (loadings −0.572, −0.767 and −0.363 respectively). Up to 33% of the variance in the immunological responses was explained by the biological data and age.

Discussion

The results of our study showed that major depressives with melancholic and/or with psychotic features showed significantly lower lymphocyte stimulation by PHA and PWM than minor depressives. Stimulation of lymphocytes by CON A tended to be suppressed in the most severely depressed patients, although this result did not reach significance. These results are in accordance with those of Kronfol *et al* (1983), Schleifer *et al* (1984) and Kronfol & House (1985), who found blunted lymphocyte responses to lectins in major or endogenous depressives. Accordingly, we found that the lymphocyte responses to lectins were significantly and negatively correlated with the severity of illness. This is at variance with the results of Kronfol *et al* (1983) and Albrecht *et al* (1985).

We found that DST non-suppressors exhibited a significantly lower lymphocyte stimulation by PHA, PWM and CON A than suppressors, and accordingly there was a significant negative correlation between post-dexamethasone cortisol values and the lymphocyte responses. These findings are at variance with those of Albrecht *et al* (1985) and Kronfol & House (1985), who found no differences between DST non-suppressors and suppressors. Also Kronfol *et al* (1986) could not find a significant relationship between free urinary cortisol and the lymphocyte responses.

According to our findings, age correlated negatively with the lectin-induced lymphocyte transformation results. This is at variance with the results of Albrecht *et al* (1985). In normal controls, some authors (Kishimoto *et al*, 1978) but not all (Portaro *et al*, 1978) found that the lymphocyte responsiveness to mitogens varied with age. Consequently, we cannot conclude whether the observed age effects are indicative of the physiological processes of ageing *per se* or whether they reflect the action of other confounding variables linked to the depressive state.

Furthermore, we found that the significant between-group differences in the immunological responses and the significant correlations with the severity of illness disappeared when the post-dexamethasone cortisol values and age were taken into account. Consequently, we tend to think that the predominant variables correlating with the blunted immune responses are hypothalamic–pituitary–adrenal (HPA)-axis activity and age, and not the severity or the subtype of depression *per se*.

In the present study we used MHPG excretion as an index of total body (central and peripheral) noradrenergic turnover (Filser *et al*, 1986). We found that MHPG excretion was related inversely with the immune parameters, particularly with the PHA stimulation results. However, the noradrenergic link is weak in view of the lack of differences across diagnostic categories. Moreover, the lymphocyte responses to the lectins had markedly weaker relationships with MHPG excretion than with HPA-axis function and age. Nevertheless, our findings of significant negative correlations between blunted lymphocyte stimulation by mitogens and the index of noradrenergic activity used are in agreement with the hypothesised reciprocal relationship between the two factors (see introduction).

Other confounding variables which might putatively affect the mitogen-induced blastogenesis were controlled for in the present study. Patients with malnutrition (Bistrian *et al*, 1975; Beisel *et al*, 1981) were excluded from our study. Putative effects of diurnal variation (Ritchie *et al*, 1983) were controlled for since blood samples were always taken at 8.00 a.m. Patients with medical illnesses known to affect the immune function were excluded (Oppenheim *et al*, 1975). All patients had been drug-free (except for benzodiazepines in some cases) for at least eight days at the time of blood sampling and we found that the concomitant low dosage schedule of benzodiazepines did not affect our results. Furthermore, patients who had received antidepressants prior to the wash-out period did not differ from the unmedicated patients in their lymphocyte responsiveness to lectins.

In conclusion, our findings of impaired lymphocyte responsiveness to mitogens in severely depressed patients can probably be attributed to a complex interface between the immune apparatus, HPA-axis hyperactivity, the ageing process and possibly noradrenergic turnover.

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The Prevalence and Patterns of Care of Huntington's Chorea in Grampian

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The prevalence of Huntington's chorea in Grampian region is high at 9.94 per 100 000. The 46 individuals (26 female, 20 male) were ascertained from 98 pedigrees. Difficulties in ascertainment, family studies, sex ratio and use of resources are discussed.

Huntington's chorea is a neurological disorder characterised by progressive chorea, cognitive impairment and emotional disturbance in which degeneration of ganglion cells of the forebrain and corpus striatum occurs. The clinical signs, which are usually evident by early middle life, progress to mental and physical incapacitation and premature death.

The definitive description by George Huntington in 1872 led to his name being given to the disease, although studies since then have established that it had been described many centuries before. Paracelsus in the 16th century subdivided chorea into three types, one of which is typical of Huntington's chorea.

The authors of the present paper considered that there could be a high prevalence of Huntington's chorea in Grampian, possibly reflecting the focus of disease known to exist in Avoch, a fishing village across the Moray Firth on the southern shore of the Black Isle (Fig. 1). This focus had been identified through the work by McWilliam (1930) and Lyon (1962).

Recent advances in recombinant DNA technology, leading to the discovery of the G8 probe (Gusella, 1983), gave impetus to the investigation and accurate ascertainment of Huntington's chorea in Grampian.

Method

The study had several objectives: to document all living, affected individuals in the region by correcting and updating the Genetic Register and thus to obtain a prevalence figure for 30 June 1984; to obtain DNA from these individuals and their spouses for storage in the event of future family linkage studies; and to provide counselling for both 'old' and 'new' families, and information for a situation in which the diagnostic probes would be available to those families requesting them. This service would thus fulfil a diagnostic and counselling role, as well as allowing access to psychiatric and social support.

The first phase of the study was to search the original data included in the Genetic Register, which contained 53 pedigree names and 108 affected individuals. Reviewing hospital and genetic clinic notes enabled the diagnosis to be confirmed and the patient's current status ascertained; all patients showed classical features of the disease. In several instances, visits to peripheral hospitals were necessary. Some additional affected family members were recognised, and their hospital notes searched for confirmation of the diagnosis.

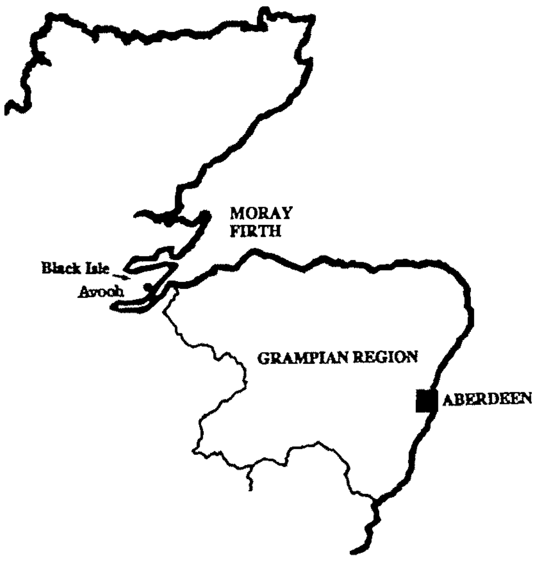

FIG. 1. Map showing area of study.

The Psychiatric Diagnostic Case Register at the Royal Cornhill Hospital, which has been in use since 1969, was also scrutinised. This was complicated by the use of several ICD codes which were changed three times during the period covered by the study. Over 100 names were produced and investigated. Not surprisingly, some individuals appeared on several code listings, and some were already known to the Genetic Register.

A search was made of Grampian Health Board's list of general hospital discharges (in use since 1970), which produced 26 patients. Not all of these lived in the region, and a doubtful diagnosis was noted in one instance.

Personal contact with the general practitioners proved invaluable when constructing pedigrees for new patients or enlarging those already known, and in some instances in collecting blood samples.

Records in the Primary Care Division of Grampian Health Board are computerised, but these records depend on an accurate date of birth. In the absence of any hospital records, this led to difficulty on occasion when attempts were made to define an individual's current status.

From the General Register Office in Edinburgh, information on place of birth was obtained on six affected individuals. An extensive search would, however, be necessary to determine the birth place of the progenitors of all the families identified.

Problems occurred when the above methods were used, the principal one being inaccurate recording of basic identifying data to allow follow-up of families. A change or lack of general practitioner also contributed to difficulty in tracing a patient. Furthermore, the social consequences of this condition often cause families to attempt to conceal their plight and therefore limit the information made available.

These problems are reflected in Table I, where four patients are listed as 'outcome unknown'.

Blood from affected individuals for storage of DNA was collected personally with prior agreement of the patient's general practitioner or consultant. In three instances an approach to the family was discouraged by the general practitioner because of the sensitive nature of the disease within the family unit. In one instance this lack of personal appraisal initially led to a faulty 'affected' label being given to an at-risk individual because of an error in the GP's patient register. At 71 years she is well and appears not to have inherited the gene.

All living patients were seen by one of the authors or a consultant neurologist.

The blood collected was initially stored at −20°C. Following extraction the DNA has been stored at −70°C. In some families, relatives living outwith our region have by arrangement attended other hospitals for blood collection and DNA has been stored there.

Pedigree information and clinical details have been exchanged with other clinical genetics departments and this has enabled scattered family units to be given as accurate counselling as possible.

Because of increased contact with the families, it was felt necessary to offer counselling in advance of the use of the predictive test. A genetic clinic has been held regularly in the Aberdeen hospitals since 1968, and families with a history of Huntington's chorea have been seen there, usually because of a newly diagnosed affected individual. However, a clinic specifically for Huntington's chorea families has now been set up because of the increased work-load resulting from the study.

Counselling those at risk involves a detailed discussion of the family history, with verification of the pedigree where possible. The use of specific DNA probes for ascertainment of status and antenatal exclusion testing is explained and discussed, and, where possible, a policy is formed for the individual. Several counselling sessions are necessary. Care is taken to exclude any clinical features of Huntington's chorea in those presenting in the at-risk category. Psychiatric and psychological assessment by Dr J. Besson is also being undertaken when individuals request the presymptomatic predictive test.

Most families welcomed the opportunity to attend the clinic after an initial approach was made via the general practitioner. The family history – if known – had quite often been kept hidden from successive generations and much anger and resentment would follow each new case in a generation.

Collyer & De Mey (1987) pointed out that a patient's knowledge of the family is often very limited, especially about the diseases from which ancestors died. This is particularly true if social stigmata are associated with a disease. Registration of birth, deaths and marriages was made compulsory in 1855, but genetic diseases are often omitted from death certificates if they do not contribute directly to the cause of death. Both hospital physician and general practitioner alike are also often ill-informed about the condition and this leads to much confused advice being given. Lack of knowledge about the current limitations of the diagnostic tests available is common. Patients also voiced their fear of being 'labelled' as an actually or potentially affected individual, with the associated implications for employment prospects, insurance, and mortgage applications. However, the opportunity to obtain accurate information, to seek counselling and to be informed about the self-help group Association to Combat Huntington's Chorea has usually been readily accepted.

TABLE I
Sources of patient data

	Psychiatric Hospitals Diagnostic Register	*Aberdeen Teaching Hospitals Diagnostic Register*	*Genetic Register*	*Totals*
Number of cases found	65	25	108	198
Patients new to genetic register	22	4	—	26
Patients' final outcome unknown	1	—	3	4
Patients alive at prevalence date	6	2	38	46[1]
Patients diagnosed since prevalence date	—	—	—	7[2]
Patients dying since prevalence date	—	—	—	8[2]

1. Includes four patients recognised at prevalence date, but not recorded on a diagnostic index.
2. At December 1987.

Results

Table I illustrates the sources and number of patients investigated in tracing the 46 patients alive at prevalence date on whom the study is based. Table II illustrates and compares the population figures for Scotland and Grampian region. Table III compares the reported prevalence in six areas with that of 9.94 per 100 000 for Grampian.

The age at death and age at prevalence date are shown in Table IV.

The results have been listed according to sex, and these figures are particularly intriguing: there are consistently more females than males in our region diagnosed as affected. This trend is present in deaths in Scotland in 1984, 1985 and 1986 reported to the Registrar General's Office, as illustrated in Table V, though for reasons given above, these figures are likely to be incomplete.

Discussion

Grampian region, consisting of the former counties of Aberdeen, Kincardine, Banff and most of Moray, is noted for its fishing and farming industries, which have ensured that village and small town communities continue to thrive. The nuclear family remains an important feature.

Some of the sufferers identified during the initial phase of the study were found to live outwith the region (e.g. in Shetland) but had attended as patients at one of the hospitals in this region. They were not included in the prevalence study, although they have made use of the genetic counselling services in Aberdeen and can be expected to continue to do so.

A cluster of five patients was found in an area served by Grampian Health Board, but just outside the regional boundary.

Prevalence

The prevalence figure of 9.94 per 100 000 is considerably higher than that quoted as a national figure, but probably is still an underestimate. In this study, unlike some others, the figure does not include patients in whom the disease was undiagnosed but who were probably symptomatic at the prevalence date as judged by their medical history. Their inclusion would raise the prevalence figure to well over 10 per 100 000. Taking an average duration of symptoms of 10–15 years, and our figure of 34 deaths in 10 years, one would expect to find 34–51

TABLE II
Population figures

Year	*Scotland*	*Grampian region*
1961	5 179 344	440 351
1971	5 228 963	438 630
1981	5 130 735	462 891

TABLE III
Prevalence rates

Country	*Area*	*Authors*	*Year of publication*	*Prevalence per 100 000*
Scotland	West of Scotland	Bolt	1970	5.2
Scotland	Grampian	Simpson & Johnston	This study	9.94
England	Northamptonshire	Oliver	1970	5.3
England	Bedfordshire	Heathfield & MacKenzie	1971	7.5
Wales	South Wales	Walker *et al*	1981	7.61
USA	Michigan	Reed *et al*	1958	4.1

TABLE IV
Age at death (deaths 1975–1984); and age distribution of those alive and ascertained at prevalence date (June 1984)

	<19	*20–24*	*25–29*	*30–34*	*35–39*	*40–44*	*45–49*	*50–54*	*55–59*	*60–64*	*65–69*	*70–74*	*75–80*	*81–84*
Deaths 1975–84[1]														
Male	0	0	0	0	0	1	1	2	2	0	2	3	1	1
Female	1	0	0	2	0	1	0	0	6	1	4	3	1	2
Ascertained at prevalence date[2]														
Male	0	1	2	1	1	1	3	1	4	1	3	1	1	0
Female	0	0	1	2	3	2	3	2	5	2	1	3	1	1

1. 13 males, 21 females; total 34.
2. 20 males, 26 females; total 46.

TABLE V

Age at death (all regions in Scotland)

	<19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
1984[1]															
Male	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Female	0	0	0	1	0	1	0	0	2	1	0	0	0	0	0
1985[2]															
Male	0	0	0	0	1	0	0	0	0	0	0	3	0	0	1
Female	0	1	0	0	2	2	1	1	3	2	2	1	0	0	0
1986[3]															
Male	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0
Female	0	0	0	1	1	0	0	1	1	0	3	0	0	2	0

1. 1 male, 5 female; total 6.
2. 5 male, 15 female; total 20.
3. 2 male, 9 female; total 11.

live affected individuals at prevalence date. This correlates well with our results. The effective prevalence figure is probably higher, since the oil industry has contributed to a population increase of more than 20 000 healthy adults in the period 1961–81, while the population for Scotland has decreased by about 50 000 (Table II).

This prevalence figure compares to some parts of South Wales, where complete ascertainment is believed to explain the phenomenon (Quarrell, personal communication). Earlier work by Walker *et al* (1981) in South Wales had attempted complete ascertainment, and produced a prevalence of 7.61 per 100 000 in the counties of Gwent and Glamorgan.

There have been several other prevalence studies in the UK (Table III) and throughout the world. Lyon (1962) stated that many difficulties had been encountered which reduced the value of the statistical examination of his material. His population base was small (896) and he included only those patients born in that area of eastern Ross-shire.

In 1970, Bolt's work in the West of Scotland estimated the prevalence as 5.2 per 100 000, and she also commented on the different presentations of the condition. In addition to patients in whom a diagnosis had been made by the prevalence date, Bolt included those whose symptoms were known to have antedated it, but in whom a diagnosis had not been made. Furthermore, not every individual had had their diagnosis confirmed.

Oliver (1970) repeated the work of Pleydell (1954) in Northamptonshire and compared the prevalence of Huntington's chorea in that area in 1954–55 and 1968–69. He obtained a figure of 5.3 per 100 000, as compared with Pleydell's 6 per 100 000. However, the population bases were different: Oliver included the county and county borough, whereas Pleydell did not include the population of Northampton borough. Oliver's comprehensive work involved searching hospital and GP files; he also circulated the county's doctors and followed Pleydell's original pedigrees. His paper had the added interest of allowing follow-up of pedigrees first noted over 12 years earlier. Oliver further commented on the devastating social consequences of the illness on affected family members, their relatives and dependants.

From work in 1972–76 in the northern part of East Anglia (the area covered by two central Norfolk mental hospitals), Caro (1977) gave a figure of 9.24 per 100 000. He observed that his prevalence rates are not strictly comparable with others owing to his different method of calculation, and compares the estimated prevalence rates from 1851–1971 by decade. This shows a substantial increase in prevalence rate (from 0.78 to 9.24), and reasons for this are suggested – such as increased reproductive fitness of gene carriers. However, he appears to have included deceased patients in his prevalence rate. The correct figure would seem to be 3.25 per 100 000. The Registrar General's figures show an increase in deaths from Huntington's chorea during this period – which may reflect better diagnosis or longer survival.

It is noteworthy that in seven of our patients the diagnosis had been made before the age of 35 years, and that there were 23 patients still alive over the age of 55 years. This suggests a much broader distribution of age of onset than is usually quoted. It is generally difficult to obtain data about age of onset: psychiatric symptoms can be the presenting feature in at least a third of cases (Hayden, 1981), and onset is difficult to assess retrospectively. Duration of symptoms, however, has been accepted as being from a mean of 10.6 years (Cameron & Venters, 1967) to a mean of 15.8 years (Reed *et al*, 1958): recent studies confirm this (Harper, 1985). Interestingly, Cameron & Venters' data give patients a range of duration of illness from less than 3 years up to 36 years, but no clinical data are given.

Sex ratio

The number of affected females is surprisingly high (57%). Possible explanations included preferential admission of females to hospital – but no unidentified males have subsequently been identified in the community; slower progression of the disease in females – but this is not supported by our data; and higher mortality in boys (Oliver & Dewhurst, 1969).

Reed *et al* (1958), discussing the demography and genetics of Huntington's chorea in Michigan, USA, showed the sex distribution of affected individuals to differ significantly from expectation – with an excess of females. The reason for this was not clear. In particular, there was not a sex difference in the mean duration of the disease, and no deficiency in the sibships. Reed *et al*'s figure (58% females) compares almost exactly with ours (57% females).

The 98 pedigrees on our Huntington's chorea register were then investigated to determine the sex ratio in both living and dead affected family members. Despite the limitations of some of the pedigrees, 141 (39.3%) affected males and 217 (60.7%) affected females were found; but among those at high risk, males numbered 223 (48%) and females 241 (52%).

Family studies

A positive family history existed in 42 of the 46 cases at prevalence date (91.3%) and in six of the seven newly diagnosed cases (83.3%). In the remaining five cases, a parent has a high index of suspicion based on diagnosis of 'Parkinsonism' or psychiatric symptoms, suicide or early death, while the patients themselves exhibit classical clinical features of Huntington's chorea.

Harper (1985) describes how much greater the impact of Huntington's chorea is than a prevalence figure would suggest because of the large number of relatives at risk: about eight times the number of those actually affected. Our own figures suggest a minimum figure ten times the number affected (46 to a minimum of 464), but only a relatively small proportion of these have been seen and counselled at the genetic clinic to date.

Six of the documented families have been clearly identified as having ancestors from Avoch. Migration of fishermen across the Moray Firth and along the coast may account for this; interestingly many of the families still live in coastal towns.

Use of resources

The impact on the health services of patients with Huntington's chorea is considerable in terms of resources used, whether these individuals are cared for in the community with help from – among others – the community psychiatric nursing service and social workers, or hospitalised.

Of the patients in this study, 50% had a social worker assigned to them; 13% were supported by the community psychiatric service.

Our experience indicates a trend, as the disease progresses, to care in hospital, with an average stay of seven years until death. The corresponding cost is £91 000 for each of these patients (1987 figures from the Grampian Health Board).

The implications of presymptomatic diagnosis are many, and patients and their families will require much support. Others (Quaid *et al*, 1987) have experienced initial enthusiasm among at-risk individuals offered the predictive test, but eventual reluctance. Our experience suggests that interest, which is initially in exclusion testing on the foetus, turns after counselling towards predictive testing.

The impact on health services of a possible decrease in number of affected individuals with their attendant costs would be significant, although the costs involved in support for a family once a positive diagnostic test has been given cannot yet be assessed. It is likely, however, that such support costs will not overshadow the considerable financial and social cost already necessary for any recognised Huntington's chorea patient and his family.

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Hyperventilation: Is It a Cause of Panic Attacks?

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During transcutaneous PCO_2 ($P_{tc}CO_2$) monitoring of 15 freely ambulant patients suffering from panic attacks, all the patients experienced a typical attack. Seven were identified as hyperventilators, as $P_{tc}CO_2$ fell to abnormally low levels during the attack. This group could not be distinguished on the basis of either their usual symptoms of panic or the hyperventilation provocation test. There was no apparent association between absolute levels of PCO_2 and the nature of symptoms. The anxiety ratings of hyperventilators were lower than those of non-hyperventilators. These data do not support the hypothesis that hyperventilation causes panic attacks or contributes to their severity. Hyperventilation may be better understood as a consequence of panic.

It has been proposed that hyperventilation is a common cause of somatic symptoms in patients with panic attacks (Lum, 1981; Magarian, 1982; Hibbert, 1984*a*; Ley, 1985). The validity of this hypothesis is of importance, not only for the understanding of disorders characterised by panic, but also for their treatment. The demonstration that hyperventilation is an important source of symptoms in panic attacks could play an important part in treatment for two reasons. Firstly, a variety of methods of respiratory control training has been reported to be effective in the treatment of panic attacks in patients thought to be hyperventilators (Bonn *et al*, 1984; Clark *et al*, 1985; Salkovskis *et al*, 1986); secondly, the catastrophic misinterpretation of symptoms of hyperventilation may act as a maintaining factor in panic attacks (Beck et al, 1974; Hibbert, 1984*b*; Clark, 1986) so that the recognition of this by the patient would be an important component of cognitive therapy.

In studies of respiratory control training, the diagnosis of hyperventilation has been based on symptom questionnaires (Garssen *et al*, 1983; Grossman & de Swart, 1984), or on the hyperventilation provocation test. The latter requires the patient to hyperventilate voluntarily and then compare the symptoms provoked with the symptoms of the panic attacks. Patients who find that voluntary hyperventilation provokes symptoms which are similar to their panic attacks are positive on the test and are diagnosed as hyperventilators. Both of these methods of diagnosis have been strongly criticised (Grossman & de Swart, 1984).

The present study employs a more direct method of assessing the role of hyperventilation in panic by continuously recording the transcutaneous partial pressure of CO_2 ($P_{tc}CO_2$), which is a measure of arterial PCO_2. Miniaturised apparatus has been used to monitor $P_{tc}CO_2$ in freely ambulant subjects experiencing naturally occurring attacks (Pilsbury & Hibbert, 1987).

In a healthy population, monitored while freely ambulant, the 99% confidence limit for maximum downward deflections of $P_{tc}CO_2$ from the mode (Pilsbury & Hibbert, 1988) was 1.05 kPa. This limit of normal downward fluctuation provides a working definition of hyperventilation and can be used as a cut-off point to distinguish hyperventilators from non-hyperventilators. An abnormal fall in PCO_2, defined in this way, is a correct, precise, and clear criterion for identifying an episode of hyperventilation, and is the measure that most closely approximates to pH change, which is likely to be the pathway by which hyperventilation can provoke symptoms (Okel & Hurst, 1961; Saltzman *et al*, 1963).

A series of patients has now been studied who have experienced typical panic attacks during ambulant $P_{tc}CO_2$ monitoring. This allows assessment of the frequency with which hyperventilation occurs during panic attacks.

Having distinguished hyperventilators and non-hyperventilators by monitoring $P_{tc}CO_2$, comparisons can be made which clarify the validity of traditional methods of diagnosis, and the extent to which hyperventilation is related to particular somatic symptoms or other clinically significant variables such as degree of anxiety, panic attack frequency, etc.

Method

The apparatus and its method of use have been described in detail elsewhere (Pilsbury & Hibbert, 1987, 1988).

Forty subjects awaiting treatment were recruited from psychiatric out-patient departments. All had been diagnosed as having panic disorder or agoraphobia with panic. The combination of patients with panic disorder and agoraphobia with panic is justified on the basis that there is no difference in the quality of panic attacks in the two disorders. The 15 patients who are presented here are those who experienced a panic attack which satisfied DSM-III criteria (American Psychiatric Association, 1980) during monitoring.

Nine patients were receiving anxiolytics or antidepressants at the time of monitoring (of whom four were diagnosed as hyperventilators in the present study), and a further three were receiving aerosol bronchodilators and corticosteroids (all of whom were hyperventilators).

Subjects attended the department for attachment of the apparatus. They were instructed in the use of a diary. The instructions were to make an entry whenever they experienced symptoms, recording (a) the severity of any anxiety (a visual analogue scale, anchored at 0 by "no anxiety" and at 8 by "very severe anxiety"), (b) the extent of their physical exertion at the time (a visual analogue scale, anchored at 0 by "none" and at 8 by "extreme"), (c) what they were doing at the time, and (d) physical symptoms experienced. They were instructed to complete the diary as soon as possible after the event if they could not do so immediately. Subjects indicated that they had experienced symptoms by pressing an 'event button' on the tape recorder. Pressing the event button left a signal at that point on the tape. Reference to the diary enabled an assessment to be made of the symptoms experienced at the time of changes in ventilation.

Following equilibration of the sensor, subjects rested for an hour, after which they were encouraged to leave the department for a walk. If they indicated that an episode of severe anxiety had occurred while they were out (indicated by a score of 6 or more on the diary visual analogue scale) *and* identified this episode as a typical panic, they were questioned, on their return, in order to confirm that the event met DSM-III criteria for a panic attack. If the walk did not provoke panic they were encouraged to expose themselves to individually selected activities or situations which were likely to do so, for instance travelling by bus or eating in public. At the end of the monitoring period patients underwent two minutes of forced ventilation of room air. They were asked to compare the similarity of the sensations induced with those of their typical panic attacks (the hyperventilation provocation test). To make this comparison they completed the Similarities Questionnaire (Clark *et al*, 1985). A positive result was indicated if they found voluntary hyperventilation 60% or more similar to their typical panic attack. This procedure allowed not only an assessment of whether or not they were positive on this test, but also confirmation of the sensitivity of the ambulant equipment to changes in PCO_2.

In addition to the measures described, patients completed a number of self and observer ratings: (a) the Hamilton Rating Scale for Anxiety (Hamilton, 1959), (b) the Marks & Mathews (1979) Fear Questionnaire, (c) a symptom check-list (Clark & Hemsley, 1982), completed with reference to a typical panic attack, and (d) the Beck Depression Inventory (Beck & Beamsderfer, 1974).

Statistical analysis

The recorded data, in analogue form, were relayed, on play-back, to the analogue to digital convertor of a computer (DEC PDP 11) which sampled the signal at intervals of 1.5 seconds real time for conversion and analysis (a detailed description of the recording and play-back facilities is given by Pilsbury & Hibbert (1988)). The digitised data were partitioned into 'bins' 0.1 kPa wide to generate frequency distribution curves, indicating the frequency with which particular values of $P_{tc}CO_2$ were recorded over the whole monitoring period. The mode and range of $P_{tc}CO_2$ values were calculated from these data. Those with recorded falls of $P_{tc}CO_2$ from the mode (the most appropriate measure of central tendency because the data were not normally distributed) of greater than 1.05 kPa were classified as hyperventilators, and the remainder as non-hyperventilators. The modal value used for this calculation was the mode $P_{tc}CO_2$ value for the whole monitoring period. Hyperventilators and non-hyperventilators identified in this way were then compared on a number of variables. Student's *t*-test has been used to evaluate the significance of differences of the means when original data are analysed, and the Mann-Whitney *U* test when the data are expressed in terms of percentage change (Armitage & Berry, 1978).

Results

The mode value of $P_{tc}CO_2$ (for the whole recording) and the size of the largest deflection from the mode (referred to as the 'fall in $P_{tc}CO_2$') during monitoring of each patient is shown in Table I, along with the response to the hyperventilation provocation test. Seven of the 15 patients showed abnormal falls in $P_{tc}CO_2$ using our criteria. In every one of these and in three of the remaining eight (cases 8, 9 and 14), the maximum fall in $P_{tc}CO_2$ corresponded in time with their panic attack. The maximum falls in the other patients did not correspond in time with the panic attack. Decrements of less than 1.05 kPa in freely ambulant subjects should not be regarded as abnormal, and if they were experiencing panic at the time this should properly be regarded as a chance association. Therefore a parsimonious interpretation of the data suggests that only 7 of the 15 can be classified as hyperventilators.

As shown in Table I, five of the seven hyperventilators and five of the eight non-hyperventilators were positive on the hyperventilation provocation test. The two groups could not, therefore, be distinguished by this test.

Table II compares the demographic characteristics of the hyperventilators and non-hyperventilators and the population means for duration of illness, panic attack frequency, and scores on the Fear Questionnaire, the Beck Depression Inventory, and the Hamilton Anxiety Scale. The hyperventilators tended to be younger and to have milder disorders of shorter duration. However, because of the range of scores in the hyperventilator group, Student's *t*-test indicated that this difference was only significant for the scores on the Hamilton anxiety scale.

Three of the seven patients identified as hyperventilators (cases 1, 4, 7) had a diagnosis of asthma for which they were receiving treatment. None of the non-hyperventilators had any diagnosed respiratory disease.

Patients described particular symptoms associated with hyperventilation experienced to a moderate or severe degree during their typical panic attacks. These symptoms included dizziness, unreality, faintness, paraesthesia, tremor,

TABLE I

The division into hyperventilators and non-hyperventilators by the size of the maximum recorded fall of $P_{tc}CO_2$ *from the mode*

Hyperventilators				*Non-hyperventilators*			
Case no.	*Mode* $P_{tc}CO_2$ *(kPa)*	*The extent of fall of* $P_{tc}CO_2$ *from mode (kPa)*	*Provocation test*	*Case no.*	*Mode* $P_{tc}CO_2$ *(kPa)*	*The extent of fall of* $P_{tc}CO_2$ *from mode (kPa)*	*Provocation test*
1[1]	6.9	3.9	–	8	7.9	0.9	+
2	5.8	3.3	–	9	7.4	0.9	+
3	6.6	1.4	+	10	6.7	0.5	+
4[1]	5.9	3.6	+	11	6.1	0.7	+
5	6.8	2.2	+	12	6.1	0.6	–
6	7.1	2.0	+	13	6.5	0.7	–
7[1]	7.3	1.4	+	14	8.4	0.8	+
				15	7.4	0.5	–

[1] Asthmatic patients.

TABLE II

Demographic and severity variables of hyperventilators and non-hyperventilators

	Hyperventilators		*Non-hyperventilators*	
	Mean	*s.d.*	*Mean*	*s.d.*
Age	39.6	14.8	46.6	13.1
Sex ratio	4F:3M		6F:2M	
Duration of illness: years	2	2	6.8	9.3
Panic attacks per week	5.4	4.4	8.3	6.5
Fear Questionnaire	66.3	50.9	106.6	32
Beck Inventory	17.6	12.9	26.4	8.8
Hamilton anxiety scale	18.1*	4.1	26	6.5

*$P<0.05$.

breathlessness, palpitations, chest pain, choking, sweating, and nausea or abdominal discomfort. Student's *t*-test indicated that there was no statistically significant difference between the two groups in the number of these symptoms complained of. However, it is striking that both groups experienced a similar high frequency of breathlessness. There was also no apparent difference in the symptoms experienced during the particular panic attack that was monitored and it was impossible, on the basis of the reported symptoms, to predict which patients had hyperventilated.

It was of interest to know whether patients, distinguished on the basis of differences in $P_{tc}CO_2$ change during panic, also showed any such differences when at rest. Taking data only from the periods when patients were resting and neither anxious nor symptomatic, mean values for mode, maximum, and minimum $P_{tc}CO_2$ for hyperventilators and non-hyperventilators were compared using Student's *t*-test. During the resting phase the range of $P_{tc}CO_2$ values was significantly greater (1.81 v. 0.73 kPa, $P<0.05$) and the minimum values achieved were significantly lower (5.86 v. 7.09 kPa, $P<0.05$) in the hyperventilators. The mean minimum value achieved by hyperventilators during the resting period was converted to an estimated arterial value (using the algorithm reported by Pilsbury & Hibbert (1987)) of 4.1 kPa, which is at the lower limit of the normal range. The mode value of resting $P_{tc}CO_2$ for hyperventilators, however, falls within normal limits.

The rate of recovery of $P_{tc}CO_2$ following voluntary hyperventilation has been proposed by Hardonk & Beumer (1979) as an additional measure to distinguish hyperventilators from non-hyperventilators. They measured the recovery of end-tidal PCO_2 three minutes after a period of hyperventilation, expressed as the percentage of mean, pre-hyperventilation, end-tidal PCO_2 level. Recovery to less than 65% of the mean pre-hyperventilation level was suggested to indicate that the patient was a hyperventilator. Using transcutaneous measures makes impossible any attempt directly to apply Hardonk and Beumer's method and measure, but an alternative measure of the rate of recovery of $P_{tc}CO_2$ after voluntary hyperventilation is the recovery of $P_{tc}CO_2$ to pre-test values three minutes after reaching the lowest value achieved during voluntary hyperventilation. The mean percentage recovery to pre-hyperventilation level achieved by the hyperventilators was 20.3% and by the non-hyperventilators was 36.4%. The Mann–Whitney *U* test indicated that this difference was significant at the $P<0.05$ level, signifying that hyperventilators showed a slower recovery of PCO_2 than non-hyperventilators.

Discussion

The cut-off point of 1.05 kPa to distinguish normal from abnormal falls in $P_{tc}CO_2$ identified 47% of the patients experiencing spontaneous panic attacks as hyperventilators during the attack. In those patients who did hyperventilate, there was no evidence that hyperventilation during a typical panic attack, of which the monitored attack was representative, was connected with any particular symptoms. The hyperventilation provocation test does not predict whether or not hyperventilation actually occurs during typical panic attacks. Furthermore, hyperventilators cannot be identified by the symptoms of previous attacks.

On the other hand, those who hyperventilate during panic can be distinguished by other aspects of $P_{tc}CO_2$ change: firstly by the rate of recovery of $P_{tc}CO_2$ after voluntary hyperventilation, and secondly, by the range of fluctuation of $P_{tc}CO_2$ and the minimum levels achieved when the patient is at rest and neither anxious nor symptomatic.

These observations suggest that hyperventilation is not associated with a particular cluster of symptoms. If this is the case, it implies that, although it occurs frequently, it does not act as a cause or important component of the typical panic attack.

Table I showed three patients classified as non-hyperventilators who showed abnormal falls of 0.8 and 0.9 kPa during the attack. Although these changes are near the upper limit of normal and coincide with panic, their significance cannot be established at this stage. However, it is apparent that falls of $P_{tc}CO_2$ during panic which exceed 1.05 kPa tend to be very large indeed and do not cluster around the normal limit. This suggests that our hyperventilators are showing a distinct response.

Three of the seven hyperventilators had diagnoses of asthma. This may have been the chance association of two common disorders. However, associations between asthma, hyperventilation, and anxiety are well documented (Hibbert & Pilsbury, 1988*b*). The frequent occurrence of asthma among hyperventilators is of great interest but, in such a small population and in the absence of additional measures of airways obstruction during panic, cannot be interpreted with any confidence in this study.

The possibility that episodes of low $P_{tc}CO_2$ might be an artifact, produced either by transient detachment of the sensor or by excessive pressure of the sensor (restricting skin blood flow under the sensor) has been excluded by preliminary investigations (Pilsbury & Hibbert, 1987). A reliable method for fixing the sensor to the skin has been established, which, although increasing the time constant of the device, does not apply so much pressure as to reduce its accuracy.

Two other aspects of the study merit consideration. First, the demands of the experimental situation may have prompted some patients falsely to report panic attacks. This is unlikely in view of the distressed state of many hyperventilators and non-hyperventilators following exposure. Secondly, there may be important differences between panic attacks from occasion to occasion. Hyperventilation may occur during some attacks but not others and the symptoms of attacks may vary significantly as a consequence (i.e. there is no typical panic attack). This possibility has not been tested in the present or previous studies, but it seems an unlikely explanation of our data, especially considering that patients had no difficulty in describing a typical panic attack, and were selected on the basis that they had had what they were happy to call a typical attack during monitoring. Quite apart from this, however, the tendency to hyperventilate appears to be a consistent feature of the individual in that hyperventilators also showed a greater fluctuation of PCO_2 when at rest and asymptomatic, and a slower recovery of PCO_2 after voluntary hyperventilation.

The latter observation suggests that, although Hardonk and Beumer's diagnostic test has been seriously questioned (Wientjes *et al*, 1984; Gardner *et al*, 1986), there may yet be some value in measures of PCO_2 recovery after voluntary hyperventilation as a means of identifying hyperventilators, perhaps in combination with measures of the stability of resting PCO_2.

Finally, it could be suggested that important changes in PCO_2, and therefore important symptoms related to hyperventilation, are being overlooked by using the size of decrements in $P_{tc}CO_2$ as the only criterion for hyperventilation. Symptoms might be provoked by changes of less than 1.05 kPa if the initial PCO_2 value is already low. However, it is unlikely that this can account for our finding of a lack of association between symptoms and a change in $P_{tc}CO_2$ because the hyperventilators in this study showed significantly lower resting $P_{tc}CO_2$ values and marginally lower modal PCO_2 values over the whole recording and yet were still not distinguished by their symptoms.

Data derived from the novel technique of ambulant monitoring of transcutaneous PCO_2 have produced several conclusions about the role of hyperventilation in panic attacks which directly contradict assumptions made and conclusions drawn in the previous literature.

The observation that approximately half the patients hyperventilated during their panic attacks is consistent with previous estimates. However, the lack of any discernible difference between the symptoms of hyperventilators and non-hyperventilators and the demonstration of the inadequacy of the conventional provocation test cast doubt on the conclusions of previous studies which have relied on symptom check-lists or the provocation test to identify hyperventilators. Our data show that hyperventilation is common in panic but is unlikely to be a significant source of symptoms in typical panic attacks. It appears to be merely a consequence of panic in individuals who may have a predisposition to hyperventilation.

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The Psychiatric Consequences of Spontaneous Abortion

TREVOR FRIEDMAN and DENNIS GATH

Sixty-seven women were interviewed four weeks after spontaneous abortion. As determined by the Present State Examination, 32 of these women were psychiatric cases. This rate is four times higher than in the general population of women. In each case the diagnosis was depressive disorder, a finding confirmed by scores on three depression rating scales. Many women showed typical features of grief. Depressive symptoms were significantly associated with a history of previous spontaneous abortion, and less so with childlessness.

Spontaneous abortion is common, occurring in about one pregnancy in five, but there have been few studies of the psychological consequences. Those there are have generally suggested that emotional symptoms are frequent after spontaneous abortion (Simon *et al*, Corney & Horton, 1974; Seibel & Graves, 1980; Leppert & Pahlka, 1984; Oakley *et al*, 1984; Wall-Haas, 1985). However, the findings have been difficult to evaluate because none of the studies used standardised measures to assess psychiatric symptoms, and some obtained information only by postal inquiry (Oakley *et al*, 1984) or by telephone (Leppert & Pahlka, 1984). In some studies the inquiry was made years after the abortion, and several studies were based on samples that were small or atypical (Simon *et al*, 1969; Seibel & Graves, 1980; Leppert & Pahlka, 1984; Oakley *et al*, 1984; Wall-Haas, 1985).

This paper reports a study in which standardised psychiatric measures were used to examine a representative sample of women four weeks after spontaneous abortion.

Methods

The subjects were a consecutive series of women who had been admitted to hospital in Oxford for complete or threatened abortion treated by evacuation of the uterus. Shortly before discharge from hospital, the women were seen by a research psychiatrist (TF) who told them about the study and its purpose. A few days later, the women received a letter from the research team offering an appointment for interview four weeks after leaving hospital.

Interviews were held mainly at the women's local health centres, and occasionally at a local hospital. The interview began with a semistructured inquiry about: previous medical, obstetric and psychiatric history; attitudes towards the index pregnancy; the circumstances of the abortion; care and information received; feelings experienced on discharge from hospital; reactions of the husband and other people; further contacts with the medical profession; and plans for future pregnancies.

Next, the interviewer assessed the patient's mental state using the Present State Examination (PSE; Wing *et al*, 1974), the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery & Åsberg, 1979), and the Hamilton Rating Scale for Depression (Hamilton, 1967).

Finally, the women completed four self-rated scales: the Beck Depression Inventory (BDI; Beck, 1967); the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975); the Maudsley Marital Questionnaire (MMQ; Crowe, 1978); and the Modified Social Adjustment Scale (SAS-M; Cooper *et al*, 1982). The latter measures overall social functioning, and functioning in areas such as job, housework, social and leisure activities, marriage, and family.

Analysis of data

Associations of psychiatric disorder with other variables (psychological, social, and obstetric) were examined by comparison of groups using Mann–Whitney *U* tests for continuous variables (for example, total scores on the PSE and neuroticism scores on the EPQ) and using the χ^2 test for categorical variables such as 'caseness'.

Results

Characteristics of the sample

Of 80 women approached, 67 attended for interview. The 13 women who refused were similar to the attenders in social class and obstetric history; five of them (38%) were single as against nine (13%) of the 67 attenders ($\chi^2 = 3.14$; d.f. = 1; NS).

The average age of the interviewed women was 29 years (range 17–42) and of their partners 32 years (range 21–50). In social class, the women resembled women of comparable age from the general population of Oxfordshire. Sixty-one women had their spontaneous abortions in the first trimester of pregnancy, and the remaining six early in the second trimester.

Of the 67 interviewed women, 46 gave no history of previous spontaneous abortion; half of this subgroup (23 women) were childless. Of the 21 women who did give a history of previous spontaneous abortion, 15 reported one previous abortion, three reported two, two reported four, and one reported five. Six of these 21 women had no children. In the full sample of 67 women, 13 gave histories of therapeutic abortions.

Psychiatric morbidity

PSE case status

The PSE relates to the patient's symptoms during the month before interview. When level five and above on the PSE Index of Definition was used to determine psychiatric case status (Wing *et al*, 1978), 32 of the 67 women were found to be psychiatric cases. This rate is about four times higher than that found among women in the general population (see under 'Discussion'). When these 32 PSE cases were allocated to diagnostic categories with the PSE CATEGO program (Wing *et al*, 1974), all were classified as having depressive disorders.

Beck Depression Inventory

The BDI relates to depressive symptoms in the preceding week. Scores on the BDI ranged from 0 to 39, with a mean score of 3.7 (s.d. 3.0) for PSE non-cases, and 15.0 (s.d. 8.2) for PSE cases (Mann–Whitney *U* test, $P<0.001$). Of the 32 PSE cases, eight could be regarded as having moderate depression (scores of 20 and above) and seven as having mild depression (scores of 15–19) in the fourth week after their abortion. In the group as a whole, the six most common BDI symptoms were: sadness (56%), irritability (55%), tiredness (52%), crying (51%), self-blame (44%), and loss of sexual interest (33%). This finding applied to all the women, and to PSE cases and PSE non-cases separately.

Montgomery–Åsberg Depression Rating Scale

Scores ranged from 0 to 36. The mean score was 4.1 (s.d. 3.3) for PSE non-cases, and 16.2 (s.d. 7.3) for PSE cases (Mann–Whitney *U* test, $P<0.001$). On the MADRS severity scale derived by Snaith *et al* (1986) from a study of psychiatric patients with depressive illness, the 32 PSE cases in the present study were divided into: recovered, 1; mild, 24; moderate, 6; and severe, 1.

Hamilton Rating Scale for Depression

Scores ranged from 0 to 25. The mean score was 3.1 (s.d. 2.6) for PSE non-cases, and 11.4 (s.d. 5.3) for PSE cases (Mann–Whitney *U* test, $P<0.001$). Five patients (7.5%) scored 17 or over, which is often taken as a cut-off for inclusion in antidepressant drug trials.

Features of grief

Many women showed features typical of the grief that commonly follows bereavement (Parkes, 1972). For example, in the first few days after abortion, 40 of the women had feelings of emotional numbness. In the next few days this numbness was followed by being 'very upset' in half the women. Several women likened the distress to that following the death of a family member. Two women took overdoses and one attempted to cut her wrists.

Twenty-five women reported feelings of guilt at having had an abortion, and 11 women rated these feelings as moderate or severe. Severity of guilt was significantly associated with PSE case status ($\chi^2=4.2$; d.f. = 1; $P<0.05$). Many of these women were distressed by thoughts that they might have caused the miscarriage in some way, typically by physical overactivity.

Twenty-four women had feelings of still being pregnant, and had to keep reminding themselves that they were no longer pregnant. Some women believed there had been a mistake in diagnosis and that they were still pregnant or had been carrying twins and lost only one of them. These thoughts of continuing pregnancy were comforting rather than distressing.

Forty-one of the women were distressed by seeing other people's young babies, and 45 by seeing pregnant women. These women found it difficult to reconcile feelings of jealousy with not wishing to harbour bad feelings.

Among women who reported a previous spontaneous abortion, many described a recurrence of the same emotions, particularly sadness, as experienced previously.

Contact with doctors

In the four weeks since leaving hospital, 46 of the women had consulted their general practitioner. Over half these women did so for emotional distress (12 with complaints of low mood, anxiety and difficulty in sleeping, and the rest with concerns about the reasons for the miscarriage).

Social functioning

Relationships with partner

On the MMQ (on which higher scores indicate worse adjustment), the overall mean score was 1.0 (s.d. 0.5) for PSE non-cases, and 1.7 (s.d. 0.9) for PSE cases (Mann–Whitney *U* test, $P<0.01$).

On direct inquiry, of the 63 women with partners, 31 reported their relationship as better since the abortion, 9 as worse, and 23 as unchanged. Twenty-five of the women described their partners as 'very upset' after the abortion; they believed this distress was more often evoked by the woman's physical experience than by the loss of the pregnancy. Fifty-one women reported received a great amount of support from their partner after the abortion.

Modified Social Adjustment Scale

Sixty-five women completed the SAS–M (on which higher scores indicate worse adjustment). The mean score was 1.6 (s.d. 0.3) for PSE non-cases, and 2.2 (s.d. 0.5) for PSE cases (Mann–Whitney *U* test, $P<0.001$).

Factors associated with psychiatric morbidity

Marital status

Psychiatric case status on the PSE was more frequent in single women (seven of nine, 78%) than in married women (25 of 58, 43%) ($\chi^2=3.8$; d.f. = 1; $P<0.05$). This difference was unrelated to childlessness or previous spontaneous abortion.

Psychological factors

(a) *Neuroticism*. The mean score on the neuroticism scale of the EPQ was significantly higher among women who

TABLE I
Previous spontaneous abortion — association with psychiatric state

Psychiatric measure (total scores)	*Previous spontaneous abortion ($n=21$)*		*No previous spontaneous abortion ($n=46$)*		*Mann–Whitney* U	
	Mean	*s.d.*	*Mean*	*s.d.*	z	P
PSE	16.76	11.17	8.57	7.06	−3.19	<0.005
Beck	13.19	9.72	7.19	6.83	−2.65	<0.01
Hamilton	10.09	5.96	5.74	5.26	−2.94	<0.005
Montgomery–Åsberg	14.95	8.49	7.57	7.05	−3.55	<0.001

TABLE II
Childlessness with previous spontaneous abortion — association with psychiatric state

Psychiatric measure (total scores)	*No previous spontaneous abortion and no children ($n=23$)*		*No previous spontaneous abortion and children ($n=23$)*		*Mann–Whitney* U	
	Mean	*s.d.*	*Mean*	*s.d.*	z	P
PSE	10.69	7.88	6.43	5.52	−1.84	NS
Beck	8.57	7.73	5.83	5.62	−1.36	NS
Hamilton	7.57	5.49	3.91	4.42	−2.51	<0.05
Montgomery–	9.48	6.63	5.65	7.09	−2.30	<0.05

were PSE cases (mean 14.1, s.d. 4.6) than among those who were not (mean 9.6, s.d. 3.3) (Mann–Whitney *U* test, $p<0.001$).

(b) *Consultation*. A history of past consultation with the general practitioner for psychiatric problems was reported more frequently by women who were PSE cases (14 of 21, 67%) than by those who were not (18 of 46, 39%) ($\chi^2=4.4$; d.f. = 1; $P<0.05$).

Obstetric factors

(a) ***Pregnancy unplanned***. There were seven PSE cases (44%) among the 16 women who said that the index pregnancy was unplanned as against 25 cases (49%) among the 51 who said it was planned ($\chi^2=0.14$; d.f. = 1; NS).

(b) *Infertility*. There were two PSE cases among the seven women with a previous history of consultation for infertility, as against 30 cases among the 60 women with no such history.

(c) *Previous therapeutic abortion*. Thirteen women reported a previous therapeutic abortion. There was no significant association between such a history and PSE case status.

(d) *Previous spontaneous abortion*. There were 16 PSE cases (76%) among the 21 women with a history of previous spontaneous abortion, as against 16 cases (35%) among the 46 women with no such history ($\chi^2=9.9$; d.f. = 1; $P<0.01$). Table I shows the mean total scores on the measures of mental state (PSE) and depression (BDI, Hamilton; MADRS). On all four measures, mean scores were significantly higher among the 21 women with a history of previous abortion than among the 46 women with no such history.

(e) *Childlessness*. Of the 67 women, 38 had children and 29 had none. There were no significant differences between these two groups on any of the four psychiatric measures.

(f) *Previous spontaneous abortion v. childlessness*. Amongst the 21 women with a history of previous abortion, 15 had children and six had none. No significant association was found between childlessness and any of the four psychiatric measures.

(g) *No previous abortion v. childlessness*. Table II shows the findings for women who had had no previous abortion ($n=46$) divided into those with children ($n=23$) and those without ($n=23$). For the childless group, mean total scores were significantly higher on the MADRS and the Hamilton scale, but non-significantly higher on the PSE and BDI scales.

Future pregnancies

Fifty women said they had been given medical advice to wait at least three months before trying to conceive again. Twelve women reported that fear of a further spontaneous abortion made them uncertain whether they would attempt to conceive again. Among 33 women who had decided to try to conceive again, 16 had decided to wait longer than the period suggested by their doctors.

Discussion

The main conclusion from this study was that levels of emotional distress were high during the four weeks after spontaneous abortion. This conclusion was indicated by the finding that 48% of the women were psychiatric cases as defined by level five and above on the PSE Index of Definition. From other studies (Wing, 1976; Surtees *et al*, 1983; Gath *et al*, 1987) it is known that, using this measure, rates of psychiatric case status are 10–12% among women in the general population and about 95% among psychiatric patients. A notable finding was that, on CATEGO analysis, all the psychiatric cases were classified as having had depressive disorders during the four weeks covered by the PSE. However, the three depression rating scales (which were administered in the last of these four weeks) showed relatively mild depression, suggesting that many of the patients were already recovering.

Many of the women attributed their symptoms to the experience of profound loss. This attribution is consistent with other findings. Thus many of the women reported symptoms typical of the grief that commonly follows bereavement. Symptoms were increased in women who had experienced previous spontaneous abortions, and this increase could be due to the cumulative effects of repeated losses. Moreover, many women were fearful of experiencing the loss of any future pregnancy.

In addition to the sense of loss, other factors may have contributed to the development of depressive symptoms. The experience of the abortion itself may have been traumatic. There is evidence that hospital admission and minor surgery can induce psychiatric symptoms (Levy, 1987). Moreover, the endocrine changes associated with spontaneous abortion may cause emotional symptoms, and here there is a parallel with childbirth.

Apart from previous spontaneous abortion several factors seem to have made women more vulnerable to these stressful experiences. Psychiatric disorder was more frequent, for example, in single women. The reason for this is uncertain, but it may have been lack of a supportive partner. As in most studies of adverse events, psychiatric disorder was found to be significantly associated with neuroticism and with a previous history of psychiatric consultation. Psychiatric symptoms were also more frequent in childless women (as might be expected), but this association applied only to women with no previous history of spontaneous abortion.

All these findings relate to assessment four weeks after spontaneous abortion. It is important to know whether in some women high levels of distress persist after four weeks. In the case of stillbirth, for example, psychiatric morbidity can persist for many months (Savage, 1988). It is also important to discover whether spontaneous abortion influences the wish for further pregnancy. These questions are being examined in a two-year follow-up study.

It is difficult to comment on indications for treatment until the findings of the follow-up study are known. However, in a study of stillbirth (Forrest *et al*, 1982) it was shown that the duration of the bereavement reaction was appreciably shortened by support and counselling which were fairly intensive. After spontaneous abortion not all women may require counselling of this intensity. However, most women visit their primary care team after an abortion, and this could provide the opportunity for explanation, advice, and reassurance, which might be beneficial in many cases.

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HIV Infection: Psychiatric Findings in The Netherlands

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A psychiatric consultation was requested in 51 in-patient cases of HIV infection. Reasons for referral included counselling, the evaluation of depressive symptoms, and the treatment of delirium. The most common DSM-III diagnoses included: delirium ($n = 13$), major depressive disorders ($n = 12$), dementia ($n = 5$), and adjustment disorders with depressive or anxious mood ($n = 5$). The psychiatric treatment of patients with HIV infection does not differ fundamentally from that of other medically ill patients with similar psychiatric symptoms. However, the psychiatric treatment of patients with HIV infection can be hampered by the fear of contagion, negative attitudes towards homosexuals and drug users, and overidentification or avoidance reactions.

In The Netherlands, AIDS (acquired immune deficiency syndrome) was diagnosed for the first time in 1982 (Prummel *et al*, 1983). By 1 July 1988, 539 AIDS patients had been registered, more than half of whom have died. AIDS is considered to be the clinical end-stage of infection with the human immunodeficiency virus (HIV). Other clinical manifestations of HIV infection include asymptomatic infection (seropositivity), acute infection, persistent generalised lymphadenopathy, and the AIDS-related complex (ARC) (Centers for Disease Control, 1986).

In addition, HIV infection may be complicated by psychogenic and/or organic psychiatric disorders (Wolcott *et al*, 1985; Fenton, 1987; Faulstich, 1987). This paper reports psychiatric findings in 51 patients admitted to the Academic Medical Centre (AMC) in Amsterdam between 1 January 1983 and 1 July 1988.

Method

The AMC is on the outskirts of Amsterdam. In addition to the Faculty of Medicine of the University of Amsterdam, it also includes a 950-bed university hospital. Since April 1986 there has been a special ward for patients with HIV infection. It initially had 10 beds, but was later expanded to 16 beds. Since June 1987, a part-time consultant psychiatrist has been available specially for patients with HIV infection. The consultations are conducted upon a telephone request from the attending physician. The consultant's findings, conclusions, and advice are transcribed to a special consultation form that is eventually included in the patient's records. As from 1986, diagnoses are made according to DSM–III (American Psychiatric Association, 1980). Based on the data noted on the consultation forms, the previous diagnoses are reformulated in DSM–III terms.

Results

Approximately 270 patients with HIV infection were admitted to the AMC. Psychiatric consultations were requested for 51 patients, excluding out-patient consultations. Of the total number of patients with HIV, 18.9% were referred for psychiatric consultation (the mean psychiatric consultation rate at the AMC was 1.2–1.5%). Three of the patients were seen by a psychiatric consultant during a previous stay in hospital, and they were counted as separate consultations.

In most of the cases ($n = 40$) the patients had already been diagnosed as having AIDS, whereas five patients had ARC (Table I).

TABLE I
Total number of HIV patients per year

	1983	*1984*	*1985*	*1986*	*1987*	*1988*[1]	*Total*
AIDS	5	2	2	6	9	16	40
ARC	0	0	0	1	2	2	5
Seropositive	0	0	0	1	2	3	6
Total	5	2	2	8	13	21	51

1. January–July 1988.

The mean age of all the patients was 37.7 (range 23–62). The group aged 35–39 was the largest, with 14 patients (27.5%); the group aged 30–34 was second largest, with 11 patients (21.6%). Most of the patients were homosexual men ($n = 45$). There were two bisexual men, and three female and one male intravenous drug user. Most of the patients were Dutch ($n = 45$) and lived in Amsterdam ($n = 33$). The mortality rate was high. As far as we know, all the 1983 patients ($n = 5$), one 1984 and 1985 patient, five 1986 patients, three 1987, and three 1988 patients have died.

The most common reasons for referral were counselling, evaluation of a depression, and treatment of delirium. Refusal of further medical treatment never constituted a reason to request a psychiatric consultation (Table II). The term 'counselling' refers to the psychiatric help and support given to patients with psychological and/or social problems. 'Differentiation between depression and dementia' refers to patients exhibiting clear evidence of dementia, whereby a depressive component is assumed. 'Evaluation of suicidal risk' was requested for one male patient who came of his

TABLE II
Reasons for referral

Reasons for referral	*AIDS*	*ARC*	*Seropositive*	*Total*
Counselling	14	2	1	17
Treatment of delirium	9	1	1	11
Differentiation between a depression and dementia	3	0	0	3
Evaluation of depressive symptoms	10	1	2	13
Evaluation of suicidal risk	1	1	1	3
Behavioural problems	0	0	1	1
Diagnostic assessment	3	0	0	3
Total	40	5	6	51

own accord to the AIDS ward, one female patient who was admitted after an attempted suicide with a heroin overdose, and one male patient with acute psychosocial problems. With respect to 'treatment of delirium', behavioural disturbances were usually implicitly the immediate cause for the requests. Behavioural disturbances were explicitly the reason for referral in the case of one patient who was addicted to drugs. He continuously ignored the rules of the ward and had violent outbursts resulting in the assault of other patients. Asking for 'diagnostic assessment' implied a request for the evaluation of the patient's mental state. For example, with respect to a patient with discrete cognitive deficiencies, the question posed was whether he was still capable of driving a car.

Each patient was visited on average three times (range 1–15). Thirteen patients had a history of out-patient psychiatric care and three patients had been admitted to a psychiatric hospital at some point in the past.

In 26 cases (51%), some functional or psychogenic complication was assumed, including 12 patients (23.5%) with a major depression. In many cases, however, it was not possible to exclude the possibility of an organic component. An organic brain syndrome was observed in 21 patients (41.2%), including 13 patients (25.5%) with delirium and 5 patients (9.8%) with dementia (Table III). None of the patients with a mood disorder were considered a suicidal risk. One patient with delirium and one patient with an organic affective syndrome exhibited manic symptoms such as elevated and irritable mood, grandiosity, and psychomotor agitation.

The psychiatric treatment of patients with HIV infection at the AMC almost always took place on the special HIV ward. In five cases, a transfer to the psychiatric ward was necessary. At discharge, one patient was referred back to a psychiatrist and five were referred to the psychiatric/out-patient clinic of the AMC.

Discussion

Since 1986 there has been a marked increase in the psychiatric consultation rate of patients with HIV infection at the AMC. This is not only related to the increased number of patients, but also to the opening of a special AIDS ward and to the participation of a psychiatrist at the weekly meetings of the multi-disciplinary AIDS treatment team. The general consultation rate at the AMC falls within the range of 0.5–9.6 reported in the literature (Hengeveld *et al*, 1984). The much higher consultation rate on the

TABLE III
Psychiatric diagnoses

Diagnosis (DSM–III)	*AIDS*	*ARC*	*Seropositive*	*Total*
Adjustment disorder with depressed or anxious mood	4	1	0	5
Atypical psychosis	1	0	1	2
Delirium	11	1	1	13
Dementia	5	0	0	5
Major depression	9	2	1	12
Organic affective syndrome	3	0	0	3
Brief reactive psychosis	3	0	0	3
Panic disorder	0	0	1	1
Uncomplicated bereavement	1	0	1	2
Diagnosis deferred on axis I	1	0	1	2
No diagnosis on axis I	2	1	0	3
Total	40	5	6	51

AIDS ward indicates that psychiatric symptoms are probably more frequent in patients with HIV infection than in other patients in a general hospital. It would seem unlikely, however, that a consultation is requested for anywhere near all the patients with possible psychiatric complications. Consequently, not much can be concluded from our findings about the incidence of psychiatric complications of HIV infection. The reported incidence of psychogenic psychiatric complications varies from 30% to 82.7%, and the incidence of organic psychiatric complications from 31.3% to 65.4% (Snider *et al*, 1983; Perry & Tross, 1984; Holland & Tross, 1985; Wolcott, 1986). To document the incidence of these complications more accurately, we intend to start a controlled prospective study of newly diagnosed patients with HIV infection.

The age distribution of the patients with HIV infection complicated by psychiatric symptoms corresponds to the age distribution reported by Bijkerk (1988) of all the AIDS patients registered in The Netherlands up to January 1988. The majority of our patients were between 30 and 45. The relatively young age in conjunction with the poor prognosis, the fear of contagion, whether rational or irrational, neurotic conflicts regarding homosexuality ('homophobia'), and prejudices against drug users can adversely affect the treatment and management of patients with HIV infection (Holland & Tross, 1985; Douglas *et al*, 1985; Cummings *et al*, 1985; Ostrow & Gayle, 1986).

The finding that the group of 40 patients with AIDS consisted solely of homosexual or bisexual men is a reflection of the fact that, in The Netherlands, AIDS is mainly diagnosed among homosexual or bisexual men (85-90%). In The Netherlands, intravenous drug users constitute 3% of all the patients with AIDS (Houweling *et al*, 1987; Bijkerk, 1988).

The reasons for referral of AMC patients with HIV infection appear to be nearly identical to the reasons recorded by Dilley *et al* (1985) and Weisman *et al* (1987). The most frequent reasons for referral reported by these authors include: evaluation of depressive symptoms or of suicide risk and behavioural disorders due to delirium or dementia. Yet, because of the differing ways they are classified, it is hardly feasible to draw any comparison. Be that as it may, our clinical experience is consistent with the view of Perry & Markowitz (1986) that the reasons for referral of patients with HIV infection are those familiar to any psychiatrist who regularly sees patients in the general hospital.

The percentage distribution of the psychiatric diagnoses of patients with HIV infection at the AMC differs only slightly from the findings of Perry & Tross (1984), Dilley *et al* (1985) and Weisman *et al* (1987). The most common psychiatric diagnoses reported by these authors include adjustment disorders with depressive or anxious mood, major depression, delirium, or dementia. As Wolcott *et al* (1985) and Detmer & Lu (1986) have already emphasised, differentiation between psychogenic and organic psychiatric complications is frequently difficult. Such symptoms as anhedonia, apathy, and the loss of weight can be indicative of a depression, a malignancy, or opportunistic infections. Moreover, it is not uncommon for a psychotic disorder eventually to prove to be a prodrome of an organic brain syndrome (Halstead *et al*, 1988; Buhrich *et al*, 1988; Schmidt & Miller, 1988). We have been impressed by the prominence of apathy and anhedonia in the context of both mood disorders and AIDS-dementia complex. Our diagnostic findings reveal neither pathognomonic nor specific psychiatric signs or symptoms, which is consistent with the conclusion of Dilley *et al* (1986).

The apparently negligible role of suicidal intentions among patients with HIV infection is striking. Only one of our patients was admitted following a suicide attempt and none of the patients with a mood disorder were considered a suicidal risk. The initial opinion in the United States was that the suicide risk would be low, and actual suicide attempts were believed to be rare (Holland & Tross, 1985). There have since been indications that the number of patients with suicidal ideations and the number of fatal suicides are increasing. Especially patients who have seen friends die from AIDS are now thought to be a suicide risk (Perry & Markowitz, 1986; Baer *et al*, 1987). Of the first 100 AIDS patients admitted to the AMC, however, five have probably died of non-natural causes (Danner *et al*, 1987).

As advocated by various other authors (Dilley *et al*, 1985; Wolcott *et al*, 1985; Perry & Markowitz, 1986), our patients with a major mood disorder were treated with supportive psychotherapeutic measures and antidepressants. Our experience with this type of psychopharmacological treatment in patients with HIV infection is ambiguous and requires further evaluation. Patients with a delirium generally responded to the usual psychotherapeutic and psychopharmacological interventions (e.g. frequent orientation, titration of external stimuli, and low-dose haloperidol). Patients with AIDS-dementia complex were less responsive to psychiatric interventions. In these patients low-dose haloperidol was sometimes helpful in reducing symptoms of agitation or anxiety.

Conclusion

The psychiatric complications of HIV infection do not include any specific or hitherto unknown symptoms or syndromes. Consequently, their diagnosis does not require any special training. On the other hand some specific knowledge is required regarding the medical aspects of HIV infection, its modes of transmission, and the special problems related to homosexuality and drug addiction.

The psychiatric treatment of patients with HIV infection does not differ from that of other medically ill patients with similar psychiatric symptoms. There are, however, several complicating factors such as the fear of contagion, whether rational or irrational, negative attitudes regarding homosexuality ('homophobia') and drug users, and the fear evoked by the poor prognosis in conjunction with the relatively young age of the patients. These factors can lead to either overidentification or avoidance reactions.

HIV infection is a chronic disease with acute exacerbations. Patients are not admitted until a long time after infection. Hence, regular contact and close co-operation with community mental health facilities, general practitioners, and agencies for psychosocial care are of essential importance.

The psychiatric treatment of in-patients should preferably take place at a medical ward of a general hospital. Close co-operation with other health care workers, including internists, neurologists, and neuropsychologists, is essential. If and when the patient's behaviour becomes impossible for the medical staff to manage, he or she should be transferred to a psychiatric ward.

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Effects of Ethanol on the NMR Characteristics of Rat Brain
Acute Administration, Dependency, and Long-Term Effects

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In rats, neither acute administration of ethanol nor the establishment of ethanol dependence by chronic administration for 28 days produced significant ^{1}H-NMR relaxation changes. However, chronic ethanol intake for six months produced a transient rise in T_1, with no change in T_2 or water content. The significance of these results for study in man is discussed and a hypothesis is proposed to explain discrepant differences between T_1, T_2 and water content. It is suggested that T_1 change with long-term ethanol exposure is related to altered free/bound water state secondary to cell membrane changes.

In vivo nuclear magnetic resonance (NMR) brain imaging has shown that the spin lattice relaxation time (T_1) of grey and white matter of patients with chronic alcoholism is significantly increased (Besson *et al*, 1981) and declines with abstinence over three months (Besson *et al*, 1986). Restoration is accompanied by a gradual improvement in certain cognitive functions. Similar T_1 measures have been demonstrated (Smith *et al*, 1985), but these are of shorter duration and attributed to dehydration effects. Acute administration of ethanol in normal subjects has demonstrated no change in T_1 or T_2 (spin–spin relaxation time) at blood alcohol levels of 46–99 mg/dl (Logsdail *et al*, 1987), but transient increases in T_1 were found at blood levels 143–197 mg/dl (Manders *et al*, 1985).

Fluorescence probe depolarisation and electron spin resonance studies have shown that ethanol has a biphasic effect on rodent neuronal membrane fluidity (Chin & Goldstein, 1977). Initially ethanol gives rise to an increase in membrane fluidity, but with prolonged exposure the membrane structure adapts and becomes more rigid. These changes are thought to be caused largely by alterations in the phospholipid composition of the membranes. Neuronal preparations from ethanol-dependent mice, therefore, show increased proportions of short carbon chain mono-unsaturated fatty acids (FAs) and a corresponding reduction in the proportion of longer-chained, polyunsaturated FAs (Littleton & John, 1977). Ethanol-induced changes such as these are of great interest since it has been proposed that altered membrane fluidity could be the mechanism underlying tolerance and dependence to ethanol and other central depressants (Hill & Bangham, 1975).

Studies on human post-mortem samples from alcoholics have also shown phospholipid changes (Tesch *et al*, 1972), while *in vivo* studies have shown an increase in the NMR spin lattice relaxation time (T_1) using data collected during proton magnetic resonance imaging of chronic alcoholic patients (Besson *et al*, 1981).

The aims of the current study are to investigate the effects of alcohol on spin lattice relaxation time (T_1), spin–spin relaxation time (T_2) and water content in rat brain regions following (a) single-dose acute administration, (b) continuous daily administration for 28 days followed by acute withdrawal, and (c) continuous daily administration for 6 months followed by withdrawal and recovery. T_1 and T_2 characterise the averaged behaviour of a group of nuclei interacting with their surroundings within a given tissue volume and as such reflect the dynamic structure and amount of water within that biological system (Mathur-De Vre, 1984).

Method

Acute single-dose ethanol administration

For the single-dose experiment, 12 adult male Sprague Dawley rats (300–350 g) were used. Six of the rats were given an intraperitoneal injection of 2 g/kg alcohol and the other six animals (used as controls) were given an injection of the same volume of the inert vehicle. After 30 minutes the rats of both groups were sacrificed and the brains dissected (Popov *et al*, 1969). Dissections were carried out 'blind' with respect to control and treated animals, and were carried out by the same investigator to ensure consistency. Cortex, mid-brain and cerebellum were removed and placed in NMR tubes for study.

T_1 and T_2 measures were made of cortex, midbrain and cerebellum using a Bruker CXP100 spectrometer at 30 °C and 20 MHz. For T_1 an inversion recovery pulse sequence was used and for T_2 the Carr–Purcell–Meiboom–Gill spine–echo sequence (Foster, 1984). Before and at the end of each session, reliability of instrumentation was checked using standard solutions of known relaxation times.

Tissue water content was calculated as a percentage of the dry tissue weight after drying at 60 °C to a constant weight over two weeks.

Ingestion of ethanol for 28 days followed by withdrawal

The 28-day experiment used 16 adult, male, Sprague Dawley rats, with a mean weight of 280 g. Eleven experimental animals were fed normal solid laboratory diet and given a solution of ethanol as the sole source of fluid. Ethanol was diluted in a solution of calf milk replacer to give a final concentration of 10% (v/w) (Corbett & Leonard, 1984). Five control animals were fed the same solid laboratory diet and provided with the milk solution minus ethanol. Ethanol intake and body weight were monitored over the 28 days of the experiment. Consumption of ethanol was 7.6–8.5 g/kg per day and body weight gains were 109 g (s.d. 12 g) and 118 g (s.d. 5 g) for the control and experimental groups respectively.

After 28 days' ethanol consumption, five control animals and six experimental animals were sacrificed by decapitation. The ethanol solution was withdrawn from the remaining five animals, which were sacrificed 12 hours later.

Ingestion of ethanol for six months followed by recovery

For the long-term experiment, 26 rats were drawn from the same group as those for the 28-day experiment, and using the same technique for six months. Twenty were fed alcohol, and were sacrificed as follows: four at six months, six at one month after withdrawal, six at two months after withdrawal, and four at three months after withdrawal. Six control animals were fed the same diet minus the alcohol, and two were sacrificed on each of the three withdrawal occasions that rats fed alcohol were sacrificed.

Statistical analysis

In all experiments, differences in T_1, T_2 and water content between groups was determined using the Mann–Whitney *U* test.

Results

Acute single-dose ethanol administration

Table I shows T_1, T_2 and water content of cortex, midbrain and cerebellum of rats treated with ethanol, and controls.

Single-dose ethanol given intraperitoneally had no effect on the T_1, T_2 or water content of either grey- or white-matter regions of rat brain. The dose administration (2 g/kg i.p.) produced a blood alcohol of 0.375% (w/v) ethanol at time of sacrifice. This level would produce gross intoxication in most human subjects.

Ingestion of ethanol for 28 days

Table II shows the effects of chronic ingestion of ethanol for 28 days, followed by withdrawal for 12 hours, on T_1, T_2 and water content of cortex and midbrain. In each case no significant changes are observed in T_1, T_2 or water in the amygdaloid cortex, midbrain or cerebellum.

TABLE I

T_1, T_2 and water content of brain regions in rats given a single dose of ethanol intraperitoneally and control animals

Group and tissue	T_1 *(ms), mean ± s.e.m.*	T_2 *(ms), mean ± s.e.m.*	*Water (% dry tissue weight), mean ± s.e.m.*
Control[1] (n = 6)			
Cortex	697 ± 5	93.0 ± 0.7	81.2 ± 0.1
Midbrain	539 ± 6	81.2 ± 0.7	76.5 ± 0.2
Cerebellum	611 ± 5	86.9 ± 0.6	78.0 ± 0.1
Ethanol[2] (n = 6)			
Cortex	689 ± 6	93.3 ± 1.0	81.8 ± 0.4
Midbrain	535 ± 3	81.2 ± 2.4	76.8 ± 0.2
Cerebellum	596 ± 5	87.0 ± 0.8	77.9 ± 0.2

1. Water, 5 ml/kg.
2. Ethanol, 2 g/kg.

All comparisons not significant (Mann–Whitney *U* test).

Daily ingestion of 7.6–8.5 g ethanol per kilogram orally for 28 days in this study did not give rise to significant change in T_1, T_2 or water content of grey and white matter either before withdrawal or 12 hours after withdrawal. The alcohol consumption corrected for weight gain tended to show a decline during the 28-day period. Furthermore, blood alcohol levels on the 28th day averaged 0.1% w/v before withdrawal, falling to 0.075% w/v at 12 hours after withdrawal. Withdrawal symptoms were mild, comprising – at 12 hours – tail-stiffening, pilo-erection and strong reactions to handling.

Ingestion of ethanol for six months

Ingestion of ethanol for six months did not in itself give rise to changes in T_1, T_2 or water content in cortex, midbrain or cerebellum. However, at one month after withdrawal there was a significant rise of T_1 in cortex (Table III), with a lesser but significant rise in midbrain T_1 value. Changes did not occur in T_2 or water content, and T_1 returned to previous (normal) levels at two months and remained at these levels at three months.

Discussion

In the experiment involving acute administration of alcohol, the blood levels achieved at sacrifice were higher than those described by Logsdail *et al* (1987), which produced no change in T_1 or T_2, and at the lower end of the range found in individuals studied by Manders *et al* (1985), which produced a rise in T_1.

The major effect of alcohol on brain NMR relaxation times follows chronic long-term (six months) exposure. The T_1 is elevated in cortex and

TABLE II

T_1, T_2 *and water content of brain regions of controls and rats fed alcohol for 28 days*

	Cortex			*Midbrain*		
	T_1 *(ms), mean* ± *s.e.m.*	T_2 *(ms), mean* ± *s.e.m.*	*Water (% dry tissue weight), mean* ± *s.e.m.*	T_1 *(ms), mean* ± *s.e.m.*	T_2 *(ms), mean* ± *s.e.m.*	*Water (% dry tissue weight), mean* ± *s.e.m.*
Control	672 ± 4.8	90 ± 1.8	80 ± 0.2	500 ± 7.8	77 ± 1.9	74 ± 0.4
Ethanol, before withdrawal	649 ± 2.4	89 ± 1.6	80 ± 0.3	495 ± 3.8	77 ± 0.5	75 ± 0.1
Ethanol, after withdrawal	669 ± 3.1	90 ± 1.4	80 ± 0.2	506 ± 2.6	77 ± 0.9	75 ± 0.3

All comparisons not significant (Mann–Whitney *U* test).

TABLE III

T_1 *of brain regions of controls and rats fed alcohol for 6 months*

		T_1 *(ms), mean* ± *s.e.m.*		
	(n)	*Cortex*	*Midbrain*	*Cerebellum*
Control	(6)	654 ± 8	486 ± 3	579 ± 6
Ethanol, before withdrawal	(4)	643 ± 9	487 ± 3	572 ± 9
Ethanol, 1 months withdrawal	(6)	703 ± 6**	504 ± 2*	579 ± 5
Ethanol, 2 months withdrawal	(6)	642 ± 4	477 ± 4	565 ± 5
Ethanol, 3 months withdrawal	(4)	650 ± 4	483 ± 9	576 ± 6

$^*P<0.05$, $^{**}P<0.01$ (Mann–Whitney *U* test).

midbrain at one month after withdrawal, and returns to pre-withdrawal levels by two months. In chronic alcoholic patients, increases in T_1 occur in grey and white matter in early withdrawal, and decline towards normal levels within three months (Besson *et al*, 1986). Therefore there are parallels in the changes in the brains of rats and chronic alcoholic patients with respect to NMR relaxation times. The fact that water content is unaltered would tend to discount the change as attributable purely to levels of tissue hydration, and the fact that water content does not change in acute administration of alcohol would discount a direct effect of alcohol as an explanation. The true curve of recovery in relaxation time is in keeping with the human *in vivo* studies showing a fall over three months following abstinence (Besson *et al*, 1986).

Chronic administration of alcohol for 28 days is likely to produce tolerance to alcohol and in this study this has occurred to a mild degree. This is not accompanied by a change in cortical T_1. Similarly, no change is present following six months' administration of alcohol. However, there is a significant increase in T_1 following recovery at one month after withdrawal. In all cases the water content does not change. The T_1 changes measured in chronic alcoholics following withdrawal and abstinence (Besson *et al*, 1981, 1986) are unlikely to arise from dehyration effects of the alcohol itself, or to be related to alcohol dependency alone – but may be linked to chronic long-term exposure and withdrawal. Based on this report, the T_1 change is unlikely to be due to water content change. Other explanations must be sought.

The hypothesis we propose is that the fatty acid composition of the inner phospholipid layers of the cell membranes is altered by chronic administration of alcohol. This alteration takes the form of a change in the ratio of saturated to unsaturated fatty acids. The consequence of this is to increase the ratio of free to bound water, resulting in increased mobility of protons giving increased relaxation times. This would occur because the physical structure of the membrane alters, changing the relationship of the protons in water with respect to the cell membrane, and reducing the mobility of the protons when influenced by magnetic excitation. This would cause an increased T_1 without a change in the water content, and may explain the changes observed *in vivo* in alcoholic patients during detoxification and abstinence (Besson *et al*, 1981, 1986).

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Olfaction and Psychiatry

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Recent clinical studies have identified significant olfactory deficits in several neuropsychiatric disorders, notably Alzheimer's disease and Parkinson's disease. These have correlated with neurochemical and neuropathological studies of the olfactory system. The presence of a specific sensory deficit may be related to the localisation of pathology within the brain. There is a need for incorporation of olfactory testing into routine clinical examination.

Olfaction has often been regarded as the "Cinderella of the senses" (Moore-Gillon, 1987). The clinical significance of the sense of smell and its disturbances has been neglected and there has been little research into the normal mechanisms or pathophysiology of smell perception by comparison with that devoted to sight or hearing.

However, recently there has been increased interest in both clinical and neuropathological aspects of olfaction, with particular consequences for psychiatry. It is important to identify the relationship of such a sensory deficit to the search for localisation of cerebral disease processes; similarly it will be necessary to incorporate into clinical practice any new developments which might add to the confidence with which diagnoses can be made.

Organisation of the olfactory system

Primary olfactory neurons arising in the nasal sensory epithelium form the olfactory nerves which pass through the cribriform plate to terminate in the glomeruli of the olfactory bulb. Here they make contact with neurons (the mitral cells) which give rise to fibres forming the olfactory tract. Mitral cell axons pass to several sites: numerically the greatest termination occurs in the pyriform cortex and adjacent corticomedial amygdala, which together form the uncus. Less heavy terminations are found in the ventral striatum (homologous to the olfactory tubercle in sub-primates), the ventromedial hypothalamus and the anterior olfactory nucleus, from where fibres pass to the contralateral bulb (Meyer & Allison, 1949; Powell *et al*, 1965; Switzer *et al*, 1985).

From these primary recipient zones, olfactory information passes to many other brain regions. The pyriform cortex projects to the thalamus (mediodorsal and medioventral nuclei) and thence to orbitofrontal and dorsolateral frontal cortex (Powell *et al*, 1965; Kievit & Kuypers, 1977; Krettek & Price, 1977; Potter & Nauta, 1979); the pyriform cortex also sends fibres to other temporal cortical areas and to the insula. It is uncertain which parts of olfactory processing are served by each pathway. It seems likely, however, that the projection to dorsal thalamus and frontal cortex, which is the major *neo*cortical olfactory representation, is involved with odour discrimination (Tanabe *et al*, 1975; Slotnik & Kaneko, 1981; Eichenbaum *et al*, 1983*b*; Staubli *et al*, 1987), cognitive aspects (Potter & Butters, 1980) and convergence with visual (Cavada, 1984) and taste (Benjamin & Akert, 1959) modalities. Olfactory pathways to the hypothalamus, which are multiple, are thought to contribute to eating and reproductive behaviour; pathways between the frontal lobes and hypothalamus may in some way integrate these functions (Nauta, 1971), although the existence of direct fronto-hypothalamic connections is uncertain (Brodal, 1981). It is unclear whether the spread to the hippocampus and to temporal cortex plays a different role from that to the frontal regions, clinical effects of lesions in both sites being similar (Rausch & Serafinides, 1975; Potter & Butters, 1980); however, hippocampal lesions may produce a greater olfactory memory defect (Staubli *et al*, 1984). As in other sensory systems, there is centrifugal modulation of olfactory input. Efferent fibres from the uncus are prominent (Powell *et al*, 1965); they terminate primarily in the olfactory bulb, which also receives centrifugal projections from the cholinergic basal forebrain (Price & Powell, 1970; Jones *et al*, 1976), locus ceruleus and raphe nuclei (Switzer *et al*, 1985).

Factors affecting olfactory performance

Before olfactory involvement in neuropsychiatric disease is discussed, certain variables which may affect olfactory function should be mentioned. Any inflammation or occlusion of the nose is likely to raise smell detection thresholds, and may persist for several weeks (Elsberg *et al*, 1935; Schiffman, 1983), so interfering with clinical testing. Smoking causes similar functional impairment, acting both through increased mucosal secretions and degeneration of the olfactory mucosa (Joyner, 1964; Doty *et al*, 1984).

The effect of ageing is particularly important in view of the findings in Alzheimer's disease (AD) and Parkinson's disease (PD) to be considered below. It is now well established that ageing is associated with a marked impairment in odour detection (Chauhan *et al*, 1987; but see Serby *et al*, 1985), intensity estimation (Enns & Hornung, 1988), identification (Schemper *et al*, 1981; Doty *et al*, 1984) and memory (Cain & Murphy, 1987). This decline with age correlates with significant degeneration of the olfactory epithelium (Smith, 1942), and of sensory neurons in the olfactory bulb (Bhatnagar *et al*, 1987), and may also relate to degeneration in central olfactory structures (e.g. Herzog & Kemper, 1980).

Another potential variable is the contribution to chemoreception made by the fifth cranial nerve. Free trigeminal nerve endings in the olfactory mucosa play a major role in perception of, and response to, irritant odours. This has been demonstrated experimentally (von Buskirk & Erickson, 1977) and in anosmic patients (Doty *et al*, 1987*a*); for example, butanol, used as an olfactory test substance, causes a marked trigeminal response (Laing, 1985). The interaction between smell and taste - apparent to any gourmet - is now being appreciated, and occurs at both peripheral (Bouvet *et al*, 1987) and central levels (Benjamin & Akert, 1959; von Buskirk & Erickson, 1977; Cain & Murphy, 1980). As a result, studies purporting to be testing purely olfactory function need to be read critically.

Olfactory changes in neuropsychiatric disorders

Alzheimer's disease

The first clinical suggestion of olfactory involvement in AD came with observations of cranial nerve function in senile dementia (Waldton, 1974). Since then, a number of reports have confirmed and extended these findings (Serby *et al*, 1985; Knupfer & Spiegel, 1986; Warner *et al*, 1986; Doty *et al*, 1987*b*; Rezek, 1987; Koss *et al*, 1988). All these studies demonstrate a marked impairment of smell identification in early AD compared with that of age-matched controls, and most also show an increased threshold for odour detection, although Koss *et al* (1988) did not find this (see also St Clair, 1984). Knupfer & Spiegel (1986) reported a greater olfactory deficit (detection, identification and naming) in AD than in cognitively similar cases of multi-infarct dementia, both groups performing worse than controls. This suggests a role for olfactory testing in differentiating AD from multi-infarct dementia, and might improve upon the Hachinski index in this regard. However, confirmation of these findings would be valuable as the controls were significantly younger than the demented groups, sex ratios were different and cognitive functions not well matched. Furthermore, as with the other studies mentioned, no pathological confirmation of diagnosis was made. The well-controlled study of Doty *et al* (1987*b*) found marked detection and identification deficits in mild AD, and, moreover, only 2 out of 34 cases were aware of their deficits, a feature not explicable by their cognitive impairment.

Recent neuropathological studies have correlated well with these clinical findings. The anterior olfactory nucleus in AD contains senile plaques, neurofibrillary tangles and reduced cell counts (Averback, 1983; Esiri & Wilcock, 1984), and the olfactory bulb also shows involvement (Esiri & Wilcock, 1984; Ulrich, 1985; Ohm & Braak, 1987), as does nasal sensory epithelium (Talamo *et al*, 1989). Associated with these morphological changes is a markedly reduced cholinergic activity in the ventral striatum (Simpson *et al*, 1984), which in common with other olfactory areas has a rich cholinergic innervation (Halasz & Shepherd, 1983). Moreover, central olfactory structures are heavily affected by AD, especially the amygdala and the entorhinal, pyriform and temporal cortices (Harrison, 1986; Pearson & Powell, 1989). It is unclear which of the lesions is most clinically significant to olfaction; it is possible that peripheral involvement (olfactory bulb and anterior olfactory nucleus) accounts for the increased detection threshold, whereas central lesions explain the identification and naming deficits. This is in agreement with the type of olfactory deficits seen in Korsakoff's psychosis (KP), mentioned below, and in temporal lobe lesions; the latter cause impaired identification and recall but do not affect detection (Rausch & Serafinides, 1975; Eichenbaum *et al*, 1983*a*).

Parkinson's disease

Odour detection (Ansari & Johnson, 1975; Ward *et al*, 1983; Quinn *et al*, 1987; Doty *et al*, 1988) and identification (Ward *et al*, 1983; Serby *et al*, 1985; Doty *et al*, 1988) are significantly impaired in PD, and represent one of the few definite sensory changes in the condition. Ansari & Johnson (1975) found this to be related to a rapid disease course, but this finding has not been replicated in later studies. The impairment appears to be independent of variables such as age, sex, medication and ratings of neurological function (Doty *et al*, 1988).

As with AD, attempts have been made to correlate the clinical picture with neurochemical and neuropathological features. Not surprisingly, in PD this has focused on dopaminergic changes (Ward *et al*, 1983), including dopamine content in the olfactory tubercle and bulb (Fallon & Moore, 1978), and in mesolimbic pathways (Javoy-Ajid & Ajid, 1980), although Quinn *et al* (1987) point out that cholinergic and glutamatergic systems could also be involved. Clinico-pathological correlations in PD are hampered by the complex relationship with AD (Quinn *et al*, 1986), and it is unclear whether the olfactory deficits in PD and AD share the same cause (Doty *et al*, 1988).

Korsakoff's psychosis

Patients with KP exhibit impaired odour detection, identification and intensity estimation when compared with non-KP alcoholics and normal controls (Jones *et al*, 1975*a*,*b*; Potter & Butters, 1980; Mair *et al*, 1986). These deficits are modality-specific and not explicable by short-term memory loss or intellectual impairment, as concurrent memory testing (Jones *et al*, 1975*a*) or other sensory identification tasks (Mair *et al*, 1986) were performed successfully. The difference in results between alcoholic KP patients and non-KP alcoholics makes it unlikely that the deficits result from trauma to the olfactory nerve.

Degeneration in the mediodorsal thalamic nucleus is the most consistent candidate neuropathological lesion in KP, and has been advocated to explain the olfactory changes, together with atrophy in the prefrontal areas to which it projects (Potter & Butters, 1980; Mair *et al*, 1986). This is supported by the reduced odour discrimination seen in experimental and clinical lesions of the prefrontal cortex mentioned previously. However, intralaminar nuclei and other sites may also be involved (Mair *et al*, 1986). Neurochemically, attention has centred on the reduced noradrenergic function in KP (McEntee *et al*, 1984), which also occurs in AD and PD (Gottfries & Roos, 1969), and which has been invoked to explain the olfactory deficits in all these conditions (McEntee *et al*, 1984).

Other neuropsychiatric disorders

There are preliminary reports of olfactory changes in schizophrenia, Huntington's chorea, Down's syndrome, and depression.

Impaired olfactory discrimination has been reported in schizophrenics when compared with medication-matched non-schizophrenic patients (Hurwitz *et al*, 1988). This phenomenon appears to be independent of psychopathological differences. Olfactory changes are perhaps not unexpected in schizophrenia, given the occurrence of olfactory hallucinations as a symptom, and the evidence linking both to temporal lobe dysfunction (Rausch & Serafinides, 1975; Roberts, 1988). It has also been found that schizophrenic men have a higher olfactory sensitivity to androsterone, a pheromone, than normal men, a difference not seen in women (Bradley, 1984). This may relate to altered sex steroid excretion profiles in male schizophrenics (Brooksband & Pryse-Phillips, 1964).

Patients with early Huntington's chorea may have impaired short-term olfactory memory, in the absence of equivalent visual or auditory deficits (Moberg *et al*, 1984). There are also symposium reports of reduced odour detection and discrimination in depression (see Serby, 1987), although this is controversial (Amsterdam *et al*, 1987) and, like the findings in schizophrenia and Huntington's chorea, awaits confirmation and further study. Finally, olfactory deficits have been reported in Down's syndrome (Warner *et al*, 1988), which is of interest given its relationship with AD (Mann, 1988). The various olfactory changes identified in neuropsychiatric disorders are summarised in Table I.

TABLE I
Olfaction in neuropsychiatric disease

	Odour detection[1]	*Odour identification*[1]	*Odour memory/recall*[1]
Alzheimer's disease	(–)	–	–
Parkinson's disease	–	–	?
Korsakoff's psychosis	–	–	–
Temporal lobe lesions	N	–	–
Frontal lobe lesions	N	–	?
Schizophrenia	?	(–)	?
Huntington's chorea	?	?	(–)
Depression	(–)	(–)	?
Down's syndrome	?	(–)	?

1. N = normal; – = clear deficit; (–) = possible deficit; ? = unknown.

Mechanisms of olfactory involvement in psychiatric disorders

The evident frequency of olfactory symptoms and signs in neuropsychiatric disorders suggests that their association is not coincidental. At present, the data provide only coarse indications of such olfactory deficits, and, to some extent, a lack of clinical sophistication limits pathological correlations. This may account for the lack of any coherent explanatory theory for olfactory involvement in psychiatric disease, with separate mechanisms proposed for each disorder; for example, acetylcholine and the olfactory bulb in AD, and noradrenaline and the mediodorsal thalamus in KP.

In principle there appear to be three main ways in which olfaction and neuropsychiatric disease may be inter-related.

First, the identification of a specific sensory deficit of this kind may help to localise pathology, a psychiatric goal which has largely remained elusive. This may become possible by more detailed correlation of sites of neuropathological involvement with types of olfactory deficit, or by a search for specific pathology indicated by clinical observation. For example, if impaired odour discrimination, but not detection, is found to coexist with pathology in the orbitofrontal cortex, then clinical identification of such a deficit will suggest disease involvement in that brain region. Correlations of this kind will require clear delineation of types of olfactory deficit, as well as separation of sensory from cognitive parameters of olfactory function. Olfactory evoked potentials, should they become available, would be valuable as an investigative tool (Moore-Gillon, 1987), particularly in AD where there are abnormal visual (Orwin *et al*, 1986) and auditory (Neshige *et al*, 1988) evoked potentials.

Secondly, the likely significance of detailed olfactory testing becomes apparent in a number of ways. It may prove that olfactory changes are present early on in disease – as is the case for AD – and might even pre-date overt psychiatric symptomatology. Olfactory testing may thereby enable earlier diagnosis and treatment. It may also be useful for differential diagnosis, such as distinguishing AD from multi-infarct dementia. Furthermore, clinical research might identify currently unknown disease subtypes with regard to olfactory involvement; for example, only a proportion of PD patients exhibit symptoms which bring them to the attention of psychiatrists. These patients might prove to be the subgroup of PD with olfactory deficits, the two features being linked by involvement of areas additional to those producing a purely motor disorder (e.g. via nigrothalamic connections or mesolimbic dopaminergic pathways). Such studies could also investigate whether olfactory changes relate to subtypes of other disorders, including depression and schizophrenia.

Thirdly, involvement of the olfactory pathways may have significant implications for disease aetiology. The possibility of nasal entry of a pathogen is currently under scrutiny for AD (Pearson *et al*, 1985; Perl & Good, 1987; Mann *et al*, 1988; Pearson & Powell, 1989) and PD (Langston, 1985). Candidate environmental toxins of this kind include aluminium (Roberts, 1986), solvents (Freed & Kandel, 1988), and pesticides (Tanner, 1989). Experimental studies have shown that significant uptake of materials occurs from nose to brain, and from the blood to the brain via leaks in the olfactory mucosa (Shipley, 1985; Balin *et al*, 1986). Both intra- and extra-cellular pathways are implicated, and constitute important breaches of the barrier between the brain and the external environment. Because of the fibre terminations of monoaminergic and cholinergic fibres in the olfactory bulb, this also represents a possible mechanism by which such structures could be involved in neuropsychiatric disease (see Hardy *et al*, 1986).

It is unclear whether the involvement of the brain areas discussed represents a vulnerability of these regions, or is merely *de facto* support for the view that dysfunction of such areas underlies psychiatric and olfactory symptomatology (see McKenna, 1987). The suspicion that a vulnerability of some kind exists has been discussed in terms of phylogenetic age: areas such as the brainstem, amygdala and pyriform cortex are considered to be pre-mammalian structures, and as such are postulated to be liable to degeneration or disease (Rossor, 1981). Alternatively, pathological processes might have a predilection for the connections from such areas to the neocortex, an evolutionary gap bridged by olfactory pathways (Reep, 1984). However, as mentioned, it is not *a priori* necessary to postulate any specific vulnerability to explain links between olfaction and psychiatric disease.

Clinical implications

Specific alterations in smell detections, identification and memory are present in a number of the major neuropsychiatric diseases (Table I). In consequence, the clinical evaluation of olfaction should become an integral part of the psychiatric assessment. Tests of olfactory function are particularly indicated in suspected dementia, where identification of deficits may be a valuable differential diagnostic sign, and such deficits may prove to antedate gross cognitive changes; tests will become more important with the advent of palliative therapy for AD. Biopsy of nasal sensory mucosa may also have a diagnostic role given the findings of Talamo *et al* (1989). Assessment should include direct questioning as well as inquiry into taste perception and enjoyment of food – as patients may be unaware of anosmia – and should be followed by clinical testing. Concurrent or recent respiratory infection or coryza should be noted and, if present, testing should be postponed or repeated when the nasal airway is clear. A smoking history should be taken and past head injury documented.

For testing, a set of fresh smell bottles is required, and examination is carried out to investigate both detection and identification. The traditional method of olfactory testing is not wholly satisfactory, especially for detection thresholds (Pinching, 1977; Moore-Gillon, 1987), but should pick up most deficits. For research purposes, the development of standardised test procedures (for example the UPSIT (Doty *et al*, 1984)) has been an important advance, as studies have used different protocols without standardisation or validation (see Chauhan *et al*, 1987; Serby, 1987). Other flaws which have affected such work include small sample sizes, poorly matched control groups, and failure to allow for the trigeminal contribution. These factors point to the need for repeated studies using larger groups and better methodology. Differentiation of deficits of detection from those of identification and memory must also be improved, particularly with regard to AD and PD, where subtle cognitive problems may compound the difficulty of interpreting test results.

It is likely that the olfactory system will continue to increase in importance to psychiatry: as part of the clinical assessment, in terms of a possible pathway for disease progression, as an aid to the identification of localised pathology, and potentially as a route for delivery of therapeutic agents.

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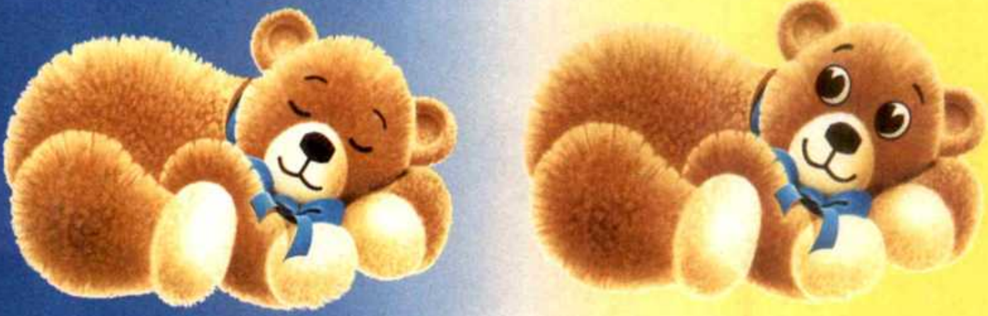

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Pharmacology Zopiclone is a non-benzodiazepine hypnotic agent, a member of the cyclopyrrolone group of compounds which is structurally unrelated to existing hypnotics and tranquillisers. **Indications** Short term treatment of insomnia. **Dosage and Administration** Adults: 7.5mg orally shortly before retiring. This may be increased to 15mg for patients who do not respond to the lower dose. Elderly: A lower initial dose of 3.75mg is recommended. The dosage may subsequently be increased if clinically necessary. Children: Not established. **Contraindications:** Pregnancy, lactation. **Precautions:** Hepatic insufficiency: A lower dose of 3.75mg nightly is recommended. Withdrawal: Used at the recommended dose abrupt termination of treatment is unlikely to be associated with withdrawal effects although patients should be closely monitored. **Interactions:** Alcohol, CNS depressants, tricyclic antidepressants. **Adverse Effects:** Mild or metallic bitter after-taste; mild gastrointestinal disturbances; minor psychological disturbances; occasionally drowsiness on waking; rarely rashes, dizziness, light headedness and incoordination. Although residual effects are rare, patients should not drive or operate machinery the day after treatment until it has been established that their performance is unimpaired. **Pharmaceutical Precautions:** Protect from light. Store in a dry place below 30°C. **Presentation and Basic NHS Cost:** (0012/0162) 28 x 7.5mg tablets £27.44. Zimovane is a trademark. Further information is available on request from Rhone Poulenc Pharmaceuticals, a division of Rhone-Poulenc Ltd., Dagenham, Essex RM10 7XS.

ABRIDGED PRODUCT INFORMATION ▼ SPECIAL REPORTING TO CSM REQUIRED

Indications: Acute and chronic psychotic states. **Dosage: Adults:** Initially 20-50mg/day in two doses. Increase over 7-10 days to 60-100mg/day in 2-4 doses. Usual maintenance dose 20-100mg/day. Maximum daily dose 250mg. **Children:** Not recommended. **Contraindications:** Use in comatose or semicomatose patients or in severe drug-induced depressed states (alcohol, barbiturates, narcotics). Known hypersensitivity to the drug. **Precautions:** May impair mental/physical abilities — patients should be warned that the ability to drive a car or operate machinery may be affected and about concomitant alcohol or CNS depressants. Use with caution in patients with:- history of convulsive disorders, cardiovascular disease, glaucoma or a tendency to urinary retention, pregnancy or lactation. **Warnings/Adverse Effects:** Extrapyramidal reactions have been reported — reduction in dosage or anti-parkinsonian medication may be necessary. Persistent tardive dyskinesia may appear after long-term therapy or when drug therapy has been discontinued. The elderly or those on high dose therapy (especially females) appear to be most at risk of this side-effect. Dystonias have been reported — dosage reduction, temporary loxapine withdrawal or corrective drugs may be required. Tachycardia, hypotension, hypertension, light-headedness, syncope, dermatitis, facial oedema, pruritis, seborrhoea, rash and anticholinergic effects have occurred. Other effects reported have included nausea, vomiting, weight-gain/loss, dyspnoea, ptosis, hyperpyrexia, flushed facies, headache, paraesthesia, polydypsia and rarely, neuroleptic malignant syndrome. **Pregnancy & Lactation:** Safe use in pregnancy and lactation has not been established. **Drug Interactions:** Interactions with other CNS depressant drugs, anti-parkinsonian drugs and alcohol may occur. **Overdosage:** Treatment is symptomatic and supportive. It should include gastric lavage and extended dialysis. **Legal Category:** POM. **Presentations and Basic NHS Prices:** Bottles of 100 Loxapac Capsules containing Loxapine succinate 10mg £9.52, 25mg £19.05, 50mg £34.27. **Licence Numbers:** PL 0095/0036-0038. Further information is available on request to the Company: Lederle Laboratories, Cyanamid House, Fareham Road, Gosport, Hants PO13 0AS. ®Loxapac is a trademark.

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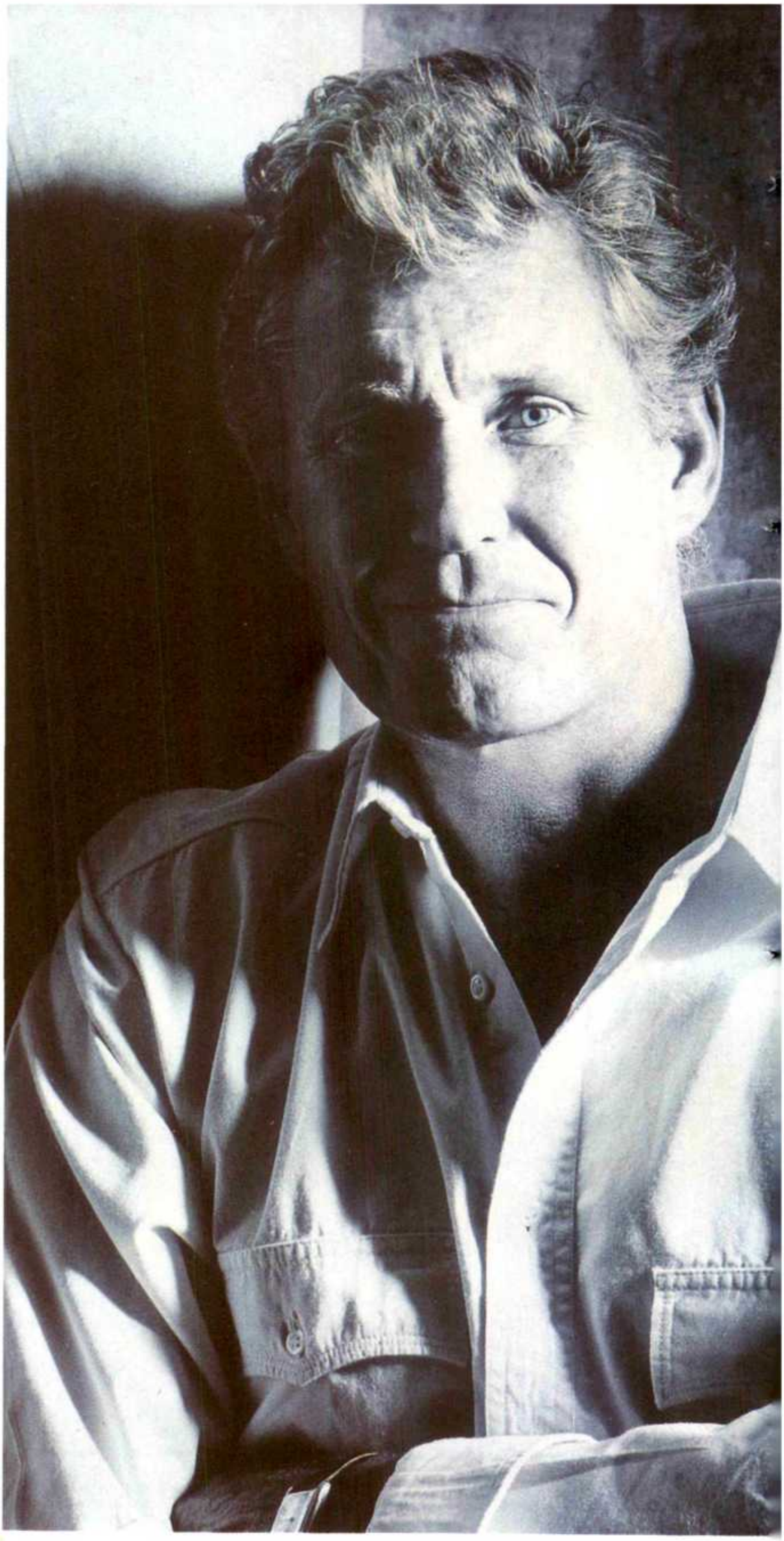
Lederle



Cool, calm and psychotic

Loxapac is a new class of antipsychotic agent which represents an important advance in the treatment of schizophrenia. Controlled double-blind studies have shown Loxapac to be as effective as haloperidol in acute schizophrenia[1], with less potential to cause troublesome extrapyramidal symptoms.[1-3].

Further controlled studies have shown Loxapac to be clinically superior to haloperidol[1], chlorpromazine[4,5] and trifluoperazine[4] in the treatment of paranoid schizophrenia. Even in patients refractory to other antipsychotic agents, Loxapac has demonstrated a high level of efficacy[6].

It has also been reported that Loxapac may suppress psychotic symptoms so well and so quickly that it may reduce hospitalisation time[7].

Thus if you want your psychotic patients to be calm and in control, choose new Loxapac to help them return to a normal, active life.

Loxapac

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NEW ANTIPSYCHOTIC

SHED NEW LIGHT

On the treatment of depressive illness

The role played by the neurotransmitter 5-HT in depressive illness is becoming more widely accepted.

So its hardly surprising that an agent that very selectively blocks synaptic reuptake of 5-HT has proved effective in the management of the symptoms of depressive illness.

Faverin is just that.

A highly selective 5-HT reuptake inhibitor.

Because its not a tricyclic, it effectively reduces the depths of depression without adding to the patients problems with unwanted anticholinergic effects – and in most cases without causing daytime sedation.

Faverin. A fresh approach to antidepressive treatment.

FAVERIN®

fluvoxamine

Highly Selective 5-HT Reuptake Inhibitor

Faverin Prescribing Information ▼ Presentation: Round, yellow, enteric-coated tablets each containing 50mg fluvoxamine maleate, imprinted with 'Duphar 291'. Pack of 60 tablets, basic NHS price £25.00. PL 0512/0070. **Uses:** The treatment of symptoms of depressive illness. **Dosage and Administration:** The tablets should be swallowed without chewing and with water. *Adults, including the elderly:* Recommended starting dose of 100mg in the evening. Adjust according to response to maximum of 300mg daily, in divided doses. *Children:* Not recommended. **Contra-indications, Warnings, etc:** Avoid during pregnancy and in nursing mothers, unless compelling reasons. Do not use with, or within two weeks of, ending treatment with monoamine-oxidase inhibitors. Faverin has been used in combination with lithium in the treatment of patients with severe drug-resistant depression. However, lithium (and possibly tryptophan) enhances the serotonergic effects of Faverin and the combination should therefore be used with caution. In hepatic or renal insufficiency use low dose initially with careful monitoring. Discontinue if associated with increased hepatic enzymes. The effects of alcohol may be potentiated by Faverin. Improvement may be delayed for two or more weeks and close monitoring is advised during this period. **Drug interactions:** Clinically significant interactions possible with drugs metabolised by liver and having narrow therapeutic index (eg warfarin, phenytoin and theophylline). Increased plasma levels of propranolol and warfarin seen in practice. No interactions seen with atenolol or digoxin. **Side-effects:** Most commonly, gastrointestinal; nausea, vomiting and diarrhoea. In some patients who report nausea, vomiting may occur. Caution should therefore be exercised when administering Faverin to patients with a medical condition likely to be exacerbated by vomiting. Others include dizziness, somnolence, agitation, headache and tremor. Anxiety reported less often. Convulsions have been reported. Avoid in patients with a history of epilepsy. Faverin may cause a decrease in heart rate; hypotension rarely reported. Further information available from: Duphar Laboratories Limited, Duphar House, Gaters Hill, West End, Southampton SO3 3JD. Telephone: 0703-472281.

(f) how regularly the medication had to be taken
(g) whether medication had ever been increased and if so, had the doctor recommended this, or had the subjects done so of their own volition
(h) the maximum number of tablets/capsules taken in a single day
(i) if the subject had stopped taking medication previously, whether they experienced any difficulties
(j) whether they had any serious medical problem that had required treatment by their physician, during the previous two years.

The full questionnaire is available from one of the authors' (GCD).

Subjects were also given a questionnaire concerned with their use of other, non-prescribed legally available psychoactive substances (alcohol, nicotine, caffeine). Results from these data are presented elsewhere (Dunbar & Morgan, 1987; Dunbar *et al*, 1988).

As might be expected from a study of this nature, the stratification system did not produce an absolutely representative data set. In the first instance however, data were considered as collected. A review of weighted data (i.e. corrected for small imbalances) was also undertaken. This made negligible difference to the findings. Thus unweighted figures are used throughout this paper.

Results

There was a 20% refusal rate in the survey. This degree of non-cooperation is typical for a Gallup omnibus survey.

From the 4148 subjects questioned there were 377 reports of benzodiazepine use, from 318 subjects; 42 subjects had received two or more different benzodiazepines during the course of the year. The past-year prevalence rate was 7.7%. The male:female ratio was 106:212 (exactly 1:2).

Data for benzodiazepine usage by age and sex are presented in Table I. The overall proportion of people receiving benzodiazepines increased with age. To facilitate data presentation by age, results were collapsed into three age bands (16–44, 45–64, and 65+). A similar pattern of usage to that described in Table I was apparent in these collapsed data. Social class seemed to have no effect on the frequency of benzodiazepine use.

As mentioned above, of the 318 subjects who reported using benzodiazepines 42 (1.0%) had used more than one drug from this family, 21 of whom (0.5%) had taken their drugs concurrently. The subjects who had used more than one benzodiazepine were asked to indicate which they considered the major therapy. Thus, 318 was the possible base for the study. However, not all benzodiazepine users were given drug-use questionnaires, largely because of interviewer error, and thus full information was available for only 295 respondents.

Of the 295 subjects who had received benzodiazepines, 151 had taken their medication in the week preceding the survey. Thus, the past-week prevalence rate was 3.6%. The male:female ratio was 94:201 (again approximately 1:2). This group of 'current users' tended to be over 65 years and most likely to be taking hypnotics. Younger subjects were more likely to be taking anxiolytics at the time of the survey.

Subjects who took their medication about with them were defined as 'carriers'. Of the 295 users 41 (14%) were carriers. Anxiolytics were carried much more frequently than hypnotics.

Subjects were also asked about whether they had medication stored at home for future use, and 197 said they had. Current users were removed from this group leaving 46 (16%) benzodiazepine 'hoarders'. Older subjects tended to collect hypnotics while younger patients tended to hoard anxiolytics. This paralleled the current user consumption pattern.

Sleep disorders, anxiety/depression or injury/epilepsy accounted for 91% of diagnoses. The remaining 9% of subjects did not know the reason for their medication.

TABLE I
Percentage of sample taking different benzodiazepines by age and sex

	16–24	*25–34*	*35–44*	*45–54*	*55–64*	*65+*	*Total*
All subjects (*n*)	813	731	690	585	563	766	4148
all benzodiazepines[1] (%)	3.6	5.6	8.0	10.3	8.9	10.8	7.7
hypnotics (%)	1.4	2.3	3.3	5.5	5.2	6.4	3.9
anxiolytics (%)	2.5	3.7	5.2	6.0	4.4	4.3	4.2
Males only (*n*)	408	355	327	267	232	373	1962
all benzodiazepines[1] (%)	4.2	2.8	5.5	7.1	6.9	7.0	5.4
hypnotics (%)	1.5	1.4	2.8	3.7	4.3	3.2	2.7
anxiolytics (%)	3.2	1.7	3.4	4.5	3.9	4.0	3.4
Females only (*n*)	405	376	363	318	331	393	2186
all benzodiazepines[1] (%)	3.0	8.2	10.2	12.9	10.3	14.5	9.7
hypnotics	1.2	3.2	3.9	6.9	5.7	9.4	5.0
anxiolytics	1.7	5.6	6.9	7.2	4.8	4.6	5.0

1. Multiple users listed once only.

Different frequencies of diagnoses were found depending on age. Thus, sleep disorders were most frequent in those over 65. This was especially the case for females. Anxiety/depression was most frequent in the young and middle aged. A peak was seen between 45 and 64 years, especially in male subjects. Sports injuries and epilepsy were most frequent in the younger age groups, especially among the males.

Data concerned with duration of treatment and the regularity with which medication was taken are given in Table II. Subjects who said they took their medication every day or almost every day were considered to be 'regular users'. The others were considered 'irregular users'. In general, regular use was more frequent than irregular use. In relation to the age bands, however, regular use was more common in the older subjects, while irregular use was more frequent in younger respondents, both males and females.

To consider further the relationship between age and benzodiazepine use, data for regular users only by age and duration are also given in Table II. A similar pattern of use was found among regular users as described for all users.

TABLE II

Percentage of subjects taking benzodiazepines for different durations and the percentage of regular users by age

	16–44	*45–64*	*65+*	*Total*
All users (*n*)	115	107	73	295
0–4 weeks (%)	38.3	15.9	2.7	21.4
1–3 months (%)	18.3	6.5	2.7	10.2
4–11 months (%)	15.7	17.8	17.8	16.9
12+ months (%)	24.3	56.1	75.3	48.5
All users (*n*)	115	107	73	295
every day/almost every day (%)	42.6	64.4	58.9	54.5
on some but not all days (%)	46.1	29.9	32.9	36.9
Regular users only (*n*)	49	69	43	161
0–4 weeks (%)	42.9	14.5	4.7	20.5
1–3 months (%)	20.4	8.7	2.3	10.6
4–11 months (%)	16.3	14.5	16.3	15.5
12+ months (%)	18.4	60.9	76.7	52.2

Percentages do not add up to 100% because of 'don't know' responses.

Considering irregular users, the longest continuous period of regular use tended to be rather short. Thus 66% of the irregular users took their medication for less than one month.

Subjects were asked if, during therapy, their medication had been altered. Of the 295 users, 65 (22%) had had their therapy changed by the doctor. In 45 (15.2%) this was initiated by their general practitioner, while the remainder asked for the change themselves. Medication was increased in 22 (7.5%) and decreased in 40 (13.6%) subjects, three subjects not knowing the direction of the change. Thus, in only 7.5% of users was there any suggestion of dosage escalation initiated by their doctor.

Subjects were also asked if they had ever wanted to increase their medication without their doctor's advice. Of the 295 users only 47 (16%) wished their medication increased. These subjects were further asked whether they had actually done so: 14 subjects had not, 31 had (11% of benzodiazepine users – two subjects could not remember whether they did or did not change their medication), but in the latter therapy was increased for less than one month in the majority of subjects (75%).

Respondents were also asked the maximum number of tablets/capsules they took in a single day. The majority (85.5%) of subjects took no more than five units in a day (low daily intake).

Data concerned with difficulty in stopping medication are illustrated in Fig. 1. Three groups were considered (a) current users, (b) hoarders (who had ceased taking medication), and (c) users who were neither current users nor hoarders (past users). Of current users, 49% had attempted termination of medication. Marked differences were found between hoarders/past users and current users, in terms of difficulty in stopping medication.

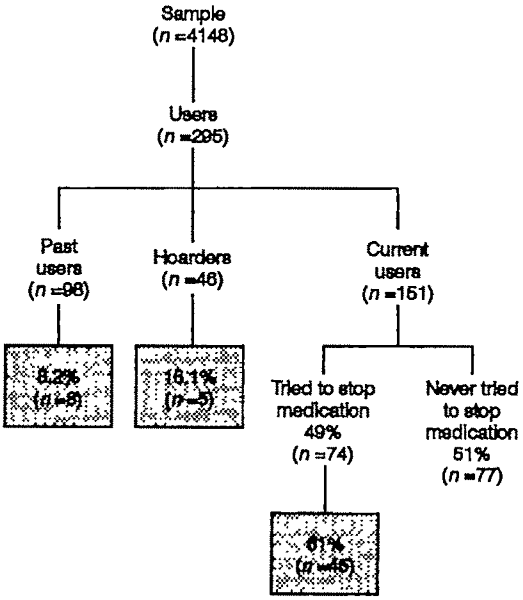

FIG. 1 Frequency of difficulties in stopping medication, indicated in figure by shaded boxes.

Of current users, 61% of whose who attempted to stop therapy had difficulties. This group principally comprised female hypnotic users; many were middle aged and 77% had been taking medication for at least 12 months. The current users who had never stopped their medication had similar characteristics except that this group contained more subjects over 65 years.

Thus, from the survey base of 295 benzodiazepine users, 58 expressed some difficulty in stopping medication.

Of these 58 subjects, 45 were current users. This suggests 15% of benzodiazepine consumers were having difficulties in stopping their therapy and as a result continued to take medication. Neither sex nor type of benzodiazepine were associated with difficulty in stopping (18% of male and 20% of female current users experienced withdrawal problems; equivalent figures for anxiolytic and hypnotics were 18% and 22%). However, duration of use was associated with difficulty in stopping medication: 5% of subjects taking therapy for up to three months, 8% taking medication for 4–11 months, and 25% of patients consuming benzodiazepines for over 12 months experienced withdrawal problems. Likewise, age was associated with difficulty in stopping: in the age group 16–44 years, 6% reported problems, while the 45–64-year-olds and those over 65 the respective figures were 22% and 19%.

Data concerned with physical illness during the two years before the survey are listed in Table III. Not surprisingly the frequency of reported illness increased with age. However, a uniform picture was seen within all age bands. Thus current users and past users reported more physical illness than non-users.

TABLE III

Percentage of subjects reporting physical illness requiring treatment by their physician within the last two years

	Current user (%)	*Past user (%)*	*Non-user (%)*
Age 16–44			
males ($n = 308$)	50	53	31
females ($n = 349$)	50	49	34
Age 45–64			
males ($n = 157$)	67	57	36
females ($n = 222$)	50	50	43
Age 65 +			
males ($n = 111$)	85	69	44
females ($n = 148$)	63	74	51

Validation

To estimate the validity of our survey, data on prescription frequency obtained from the DHSS were used as an external criterion. Products were listed in rank order and compared with the reported frequency of use from the study. A good concordance was seen (Spearman rank correlation coefficient 0.903; $P < 0.002$), suggesting the survey was based on a representative sample of benzodiazepine users.

As indicated earlier, the present survey detected a past-year prevalence rate for benzodiazepine use of 7.7%. In his survey conducted in 1981, Balter *et al* (1984) found a past-year prevalence rate of 9.4%. This represents approximately an 18% reduction of benzodiazepine use. Official prescription figures show a 13% reduction over the same period (29.4 million in 1981 and 25.7 million in 1985). Thus good agreement can be seen in the trend detected between the surveys and the reduction in absolute prescription figures.

As a further check on data validity, the type of benzodiazepine use reported was cross-tabulated with patient's reported diagnosis. A 73% concordance was found between the type of benzodiazepine used (anxiolytic or hypnotic) and the diagnosis of anxiety/depression or insomnia. Also, over twice as many subjects reported using anxiolytic rather than hypnotic-type drugs for sports injury/epilepsy. This suggests a good degree of comprehension on the part of the subjects, in terms of their therapy. It also indicates subjects were responding coherently, thus adding further to the face validity of these findings.

Discussion

Conclusions based on the present survey must be regarded with some caution, since this type of data can be flawed by poor sampling, poor interview technique, and/or poor respondent performance (Wilson, 1981). The refusal rate was 20% and clearly this non-cooperation could have produced a sample bias. However, any such bias was unlikely to be specific for the present questionnaire, since refusers had no idea as to the content of the declined interview items. Once the interview was initiated, bias towards the benzodiazepine topics was reduced since the questions were presented alongside other items concerned with political views and consumer products.

When compared with Balter *et al*'s (1984) survey performed in 1981, it appeared that a real decrease in usage had taken place (from 9.4% to 7.7%).

Considering the frequency of usage, benzodiazepine intake broadly speaking increased with age (Table I). Anxiolytics were used more often than hypnotics by the young and a peak incidence was found in middle age. Hypnotics were used more often by the elderly. Both of these patterns of use were most evident in females. The high incidence of anxiolytic use in young males aged 16–24 was due to sports injuries.

During the previous year 42 people had received more than one benzodiazepine, and of these, the 21 subjects who were taking two or more benzodiazepines concurrently may reflect multiple prescribing, which should not have been occurring.

The concepts of 'carriers' and 'hoarders' were not found to be useful. Carriers took anxiolytics with them more frequently than hypnotics, but this might simply reflect the three-times-a-day dosing schedule often used by physicians for this type of drug. However, the carrier concept was also explored to see if the clinical notion of subjects taking their medication out with them to use on an 'as-required' basis was in fact valid. The present findings do add some support to the idea, but this type of usage cannot be common, since only 14% of the sample actually took their medication out with them.

When duration of benzodiazepine use was considered, a very clear age-related pattern emerged. Thus, the younger the subject, the shorter the likely duration of treatment. The overall findings for duration of regular use were compared with those of Balter *et al* (1984) and were found to have increased between the surveys. Thus, in 1981 27.4% of subjects had taken their medication regularly for over 12 months, while in 1985 the equivalent figure was 52.2%. This was interesting, since over the four-year period actual population consumption of benzodiazepines had decreased, as had the user past-year prevalence rate. One explanation for this could have been the growing awareness, among physicians, of the need to avoid benzodiazepine therapy, or to keep courses of treatment short. Thus, new subjects would have received either no drug treatment or short-term therapy only. However, if there remained within the population a core of chronic users who could not stop taking their drug, then they would have accounted for this increasing proportion of long-term users.

Only 7.5% of subjects had their dosage increased by their doctors. This suggests that tolerance, as reflected by dosage escalation, does not often occur with benzodiazepine usage. Sixteen per cent of respondents had felt the need for an increase in medication, and in fact 11% of users did so for short periods without their doctor's advice.

High-dose benzodiazepine abuse was uncommon; however, six subjects were using more than ten units a day, suggesting a few subjects might have been misusing their medication.

Dosage was increased without the doctor's approval by 10 subjects with high daily intake and 21 subjects with low daily intake. This approximate 1:2 ratio was three times in excess of what might be expected from sample characteristics (high intake:low intake = 1:6). The excess number of high-intake subjects who experienced dosage escalation lends support to there being a small group of benzodiazepine users showing the more classic features of dependence.

Overall, 58 subjects experienced some difficulty in stopping medication. However, it was current users who were much the most likely to have experienced these difficulties (Fig. 1).

The association between current use, withdrawal problems, and chronic consumption (77% of current users who had experienced withdrawal symptoms had been taking medication for over 12 months) represents an important finding. It lends support to the notion that events during termination of therapy might have initiated long-term usage. The nature of these events was not explored in the present survey, but the most likely explanation of the difficulties is the reappearance of illness symptoms or the appearance of withdrawal features. If difficulty in stopping medication equated with withdrawal symptoms, then clearly the present findings suggest at least 1.1% of the population was dependent on benzodiazepines (as measured by difficulty in stopping, plus current usage, plus chronic consumption). This conclusion is supported by literature findings (Tyrer *et al*, 1981; Petursson & Lader, 1981). However, some caution must be observed. Other authors (Mellinger *et al*, 1984; Marks, 1980; Rickels *et al* 1985; Uhlenhuth *et al*, 1988) found that long-term benzodiazepine therapy was often used appropriately for the control of chronic symptoms. Whatever the explanation, the present study clearly identified a core of chronic benzodiazepine users who had experienced difficulty in stopping their medication.

It was interesting to note the association between benzodiazepine use and physical illness (Table III). Across all age bands, current users and past users reported more physical illness than non-users. As outlined above, this would lend support to the notion that medication was being used for the amelioration of chronic symptoms, although hypochondriasis might be compounding the results. A further explanation might simply be that physical illness was associated with anxiety and sleep disorders.

Literature sources have mostly been concerned with the chronic use of anxiolytics and the associated difficulty in stopping medication. The present findings suggest that if chronic use is a problem, then it is as frequent in hypnotic users as in those patients receiving anxiolytics.

Acknowledgements

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Studying the 'Grammar of Psychotherapy' Course Using a Student and Control Population

Some Results, Trends and Disappointments

STUART LIEBERMAN, JOHN COBB and CORAL H. JACKSON

In a study of the effects of the teaching of the 'Grammar of Psychotherapy' Course, 26 subjects were matched with 27 controls. The students were found to have significantly better interviews than the controls as rated by their patients and by independent blind assessment of their audiotapes six months later. There are some trends which were of interest, although not statistically significant.

The 'Gramar of Psychotherapy' Course initially teaches simple interview competence. After this basic work students are encouraged to concentrate on more complex psychological and interactional skills. The course involves 13½ hours of teaching spread over nine months (Lieberman & Cobb, 1987; Cobb & Lieberman, 1987). The Grammar of Psychotherapy Course was developed with four aims: to teach communication skills, to increase awareness of psychological factors in psychiatric practice, to introduce a range of psychological treatment strategies, and to provide a model for self-monitoring through the use of audiotape feedback. The course comprises nine 1½-hour seminars. Three introductory seminars concern three self-monitoring instruments ('interactograms') which address three different levels of interaction. Seminar 1 exposes the student to basic communication skills, seminar 2 examines the student's aims and intentions, and seminar 3 focuses on the ability of the student to hypothesise and to recognise transference and countertransference phenomena. The next five seminars are audiotaped supervision sessions. The first six seminars occur on six consecutive weeks. The last three seminars are consolidation sessions taking place six months later.

The course philosophy is that the relationship between the doctor and the patient should be examined by all trainees in a systematic way. As far as possible, no value judgements were made about what was 'right' or 'wrong' about an individual's interview style. Instead we applied the criterion of effectiveness judged both from the doctor's and the patient's point of view.

This study examines the effectiveness of such a relatively short course in producing measurable change in the way students interview patients by comparing students with matched control subjects.

Systematic evaluation of a teaching package has been done before (Maguire *et al*, 1984) but rarely as a controlled study. This research does not easily lend itself to the collection of data and is fraught with difficulties. There is a need to attempt systematic evaluation of such a package. The problems of measurement began with obtaining two similar groups of subjects, given the nature of our peripatetic teaching task. Measurements of success are also problematic. Providing a successful interview from the patient's point of view requires qualities quite different from those needed to satisfy trainers or consultants. Junior psychiatrists are exposed to various training courses over which we had no control.

Our aim was to study the effect this course would have on the interviews our students conducted with their patients. Were we able to prove our course could teach simple interview skills? Was there any evidence that complex interactional insights such as increased psychological sensitivity and awareness of the importance and complexity of therapeutic relationships were in any way enhanced by our course?

Method

Our students and controls were drawn from the junior psychiatrists of the South West Thames Region. They were allocated according to the hospital in which they were working at the time of the study.

Assessments of the students were done before the beginning of the course, after the sixth session (at six weeks) and after the ninth session (at six months). Control subjects were likewise assessed initially and at six weeks and six months. All assessments were done by a research psychologist who attended and audiotaped patient interviews of all subjects and controls as well as observing and recording their non-verbal behaviour. Patients were asked to rate the interview afterwards. Each student was given a multiple-choice examination after the first three seminars to determine their understanding of the course material presented.

Data analysis was done blind whenever possible. None of the data were analysed until after the end of the study period. Whenever possible two interviews were taped and the five-minute extract for analysis was taken from the second interview to allow the doctor to familiarise himself with the situation. The audiotapes were given to an assistant who recorded five-minute segments from them onto numbered tapes and ensured that details identifying the doctor in question were removed. Each taped segment was randomly included on compilation tapes which were then jointly rated by the authors. Non-verbal observations were coded by the research psychologist.

All data were collected and computerised for analysis using SPSS.

Subjects

Twenty-seven junior psychiatrists (23 male, 4 female) acted as controls. There were 26 course students (22 male, 4 female). There was no significant difference in the two groups insofar as sex, medical school attended, previous psychotherapy experience, or examination results were concerned, but the control group had been junior psychiatrists for 1.15 years (s.d. 1.4), while the course students averaged 2.19 years (s.d. 1.55; $P<0.01$). The course students were also older (32.9 years, s.d. 6.6; $P<0.01$) than the control group (age = 29.7, s.d. = 0.4). The course students attendance averaged 7.6 sessions.

Results

The patients were asked to rate the doctor's interview ability on ten different parameters (see Table I). The scores were combined and the means were tested using a one-tailed t-test, after the scores were adjusted so that the pre-course scores were used as the baseline measure and the differences between the mid-course and post-course means were analysed (Table I). The control group had deteriorated in their interview at six weeks ($x = -84.24$) compared with the students, whose performance also deteriorated but by a smaller amount ($x = -13.86$). This difference was statistically significant ($P<0.01$). By the end of the six months, the control group was still below baseline measurement ($x = 38.04$) while the student group were rated as modestly improved ($x = 19.07$). This difference was also statistically significant ($P<0.01$).

The audiotaped interviews were rated on eight different parameters scoring from 0 to 5 and these scores were adjusted so that pre-course scores were used as the baseline measure and the differences between the mid-course and post-course means well analysed (Table II). At six weeks there was no significant difference between the control and course students, but at the end of the six months the interviews of the students ($x = 0.32$) were found to be significantly better ($P<0.02$) than the controls ($x = 0.04$).

Hypotheses (i.e. the student's formulation of the patient's problem) on the taped interviews were classified into five broad categories: diagnostic, biological, intrapsychic, interpersonal, and social. There was no significant difference between groups in the type of hypothesis used either when the data were analysed in two broad categories

TABLE I

Patients' rating of doctors' interviews: differences of scores from baseline at six weeks and six months

	Feelings before your interview	*Do they facilitate*	*Can they be trusted?*	*Do they listen?*	*Are they understanding?*	*Do they show interest?*	*Are they sympathetic?*	*Do they interrupt?*	*Do they look at you?*	*Feelings after the interview*
Six weeks										
control	6.8	11.2	−12	−2.1	−11.9	−0.09	−7.3	−13.3	−0.7	−11.8
students	9.6	−0.2	3.7	−11.2	−2.2	−2.9	1.7	−8.5	−6.1	2.3
Six months										
control	−2.7	−7.1	3.3	−2.2	−3.7	−5.7	0.2	−15.1	−5.9	0.8
students	12.5	3.9	3.6	0.3	0.7	−2.2	1.6	−5.5	−1.5	2.7

TABLE II

Observer ratings of doctors' interviews: differences of scores from baseline at six weeks and six months

	Does the doctor like the patient?	*Does the doctor listen?*	*Is the doctor sensitive to patient issues?*	*Is transference present?*	*Is the doctor aware of transference?*	*Assessor's impression of the doctor*	*Did the interview benefit the patient?*	*Global rating of interview*
6 weeks								
control	0.3	−0.1	0.3	−0.04	0	0.04	0.1	0.2
students	0.1	−0.4	−0.1	0.4	0.2	−0.2	−0.1	−0.04
Six months								
control	0.04	0.1	0.3	−0.3	0.4	−0.03	−0.2	0.1
students	0.04	0.3	0.5	0.2	0	0.2	0.5	0.6

(biological v. psychological) or when analysed in separate categories.

The types of intent included giving of information, prescribing, confronting, catalysing, catharsis, support, and seeking information. There was no significant difference in the type of intent used in the interviews, nor was there a significant difference in the rating of the effectiveness of their intent. There was a trend present in which the control group used prescription more at the end of the six months than they had at the beginning, while the students decreased their prescribing intent during the course of the study. The least represented intent in both groups was catharsis.

There was no significant difference in the non-verbal scores although the trend was towards greater non-verbal synchrony between student and patient (four times that of controls) at mid-assessment and seven times that of controls at post-assessment.

The students average score was 65% on multiple-choice test of 75 questions.

Analysis of the interventions showed no significant overall difference.

Discussion

Our most striking result was the effect the course had on the way that patients rated their doctors. Both groups were perceived to have provided poorer interviews after six weeks, but the control group was four times worse than the students and eight times worse than their baseline. We expected that the course might temporarily worsen the interviews of students as they struggled to absorb, master, and integrate the new interventions, intents, hypotheses, and awareness emphasised in the course. Students were warned that just as coaching in sports such as tennis can lead to a temporary worsening of overall performance the effect of this course might be similar. However, the control group showed a far greater worsening of their rating by patients than the students. We are not sure of the reasons for this. Junior psychiatrists must learn to deal with new knowledge, check-lists, and insights when dealing with psychiatric patients. Perhaps the course enabled students to retain or develop ways of interviewing valued by patients while integrating the new knowledge of the psychiatric framework. Those junior psychiatrists not taking our course may have had a greater struggle in integrating the new knowledge into their existing interviewing repertoire. The multiple-choice results indicate that the students did learn the information provided in the course.

At six months the students improved their scores above baseline whereas the controls remained four times worse than when they started. This suggests that the students did need time to digest new ideas and attitudes before they became incorporated in a natural interview style. A reasonable conclusion is that this course had a positive effect on the way patients perceived their doctors during interviews.

The trainers did not need to spend a long time teaching and supervising. Perhaps the audiotape feedback helped the students; working on their own with 'interactograms' to guide them may have helped them acquire basic psychotherapeutic awareness and attitudes. Courses such as this one may decrease the time necessary for students to integrate basic psychotherapeutic understanding with general psychiatric skills.

The results of the observer ratings of the taped interviews seem to confirm the patient's perceptions of their doctor's interviews. Our criteria for rating the tapes were those which we believed most psychiatrists would accept. For example, students should like their patients, listen to them attentively, and the patient should feel that the interview has been beneficial. Goin & Kline (1974) reported that good supervision is primarily perceived by trainee psychiatrists as being related to learning attitudes and technique with a patient focus.

We were unable to find any statistical support for our expectation that students would learn specific skills. For example, we expected that the course would increase the likelihood that students would make more intrapsychic and interpersonal hypotheses after training, but our data showed no significant results. Perhaps the number of subjects was too small to detect a difference. It is possible that a short course cannot achieve this goal of increased psychological conceptualisation. We may not have emphasised this aspect enough in our training, or it may be more difficult to learn than we assumed.

One of our intrinsic assumptions was that the wider the skill of the doctor the more effective they would be. There was no support in our data for this assumption. In relation to the doctor's intent in the interview, medically trained doctors were good at prescribing. Psychiatrists need to broaden their ability to pursue the full range of different intents. One trend in our data showed that our students appeared to have made a start towards curtailing their use of prescription. Evidently they need more help than this short course can provide in the use of intents such as catharsis.

Our control group was three years younger and had one year less experience in psychiatry than our students, but we compensated for these differences by using the baseline data for each group as the zero point in our data analysis.

Allowing for the difficulties of evaluation mentioned in our first paper (Cobb & Lieberman, 1987) we were encouraged by the results of this study. There is evidence that a structured short course, economical of time, can make a significant contribution towards increasing the psychotherapeutic awareness of general psychiatrists. Anecdotally, students who attended the course commented that they found our introduction to this field valuable and engaging.

Our disappointment with the lack of firm confirmation of the learning of specific skills is tempered by the hope that further analysis of the data is possible and may provide more clues as to the validity and significance of trends in the data, some of which are reported.

The simplicity of this course lends itself to the possibility that general psychiatrists could teach it with minimal training and therefore further integrate psychotherapeutic expertise into general psychiatric practice.

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Point of View

Aggressiveness, Anxiety and Drugs

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Aggression and anxiety are among the most common phenomena needing medical control, especially in acute mental disorders. Today we can choose from a confusingly large array of drugs which can quickly control these two kinds of emotional and behavioural disorders. Everyday practice shows that these two groups of symptoms, seemingly so different from one another, can be treated with the same drugs. If we probe more deeply into the matter, we find that the similarities in these effects include not only inhibition of aggressiveness and anxiety but also their enhancement, activation, and provocation. These effects seem to form a regular pattern: those that increase aggressiveness (sympathicomimetics, catecholamines, 'activating' antidepressants, psychostimulants, and anti-Parkinsonics (cholinolytics)) also tend to increase anxiety, while those that decrease aggressiveness (beta-blockers, neuroleptics (major tranquillisers), 'sedative' antidepressants, minor tranquilisers, hypnotics, analgesics, and anticonvulsants) also tend to decrease anxiety.

There are two types of exceptions to these effects. A dose much higher than the standard therapeutic dose can produce an opposite effect, a phenomenon inherent to many other drugs. Secondly, an abnormal terrain (e.g. the presence of damage of the central nervous system) can cause bizarre or unusual sensitivity responses, with the risk of precipitating paradoxical reactions.

That such different groups of symptoms are both controlled in nearly the same way needs an explanation. This explanation could be quite simple. Fear (anxiety) and fighting (aggression) are the most ancient responses of living beings when faced with danger or when meeting something unknown and new. Ethologists, neurophysiologists, and other researchers have demonstrated a very meaningful fact: fear turns to fighting very easily and vice versa. This reversible process can easily be explained if one bears in mind that at the root of anxiety and aggression lies the basic activity of the central nervous system. This activity is at the same time spontaneous and unceasing – it arises from the normal functioning of the neuron itself.

Other data also point to this hypothesis. For example, some psychosocial factors that diminish both aggression and anxiety are caressing, faith, love, the forming of groups, hierarchical order, and motor activity, while some of the factors activating or increasing both phenomena are isolation, deprivation of a motivating object, helplessness, frustration, threat, pain, and territorial intrusion.

These considerations allow the formulation of a rule: if a drug has anti-aggressive effects, one can rightfully expect that it will also have anti-anxiety effects and vice versa: the most anxiolytic drugs often show anti-aggressive effects as well. This rule could help medical practitioners when choosing from the confusing abundance of psychopharmacological agents. The exceptions have to be borne in mind, but they do not invalidate the rule.

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Brief Reports

Paedophilia and Hyperprolactinaemia

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The case of a man presenting with paedophilia who has found to be hyperprolactinaemic is described. There is possibly a link between paedophilia and endocrine disorders.

Men with hyperprolactinaemia have a high incidence of sexual problems, with loss of libido, erectile dysfunction, and ejaculatory failure occurring in 50–90% (Carter *et al*, 1978; Franks *et al*, 1978; Bouloux & Grossman, 1987). Moreover, raised prolactin was discovered in 6% of men attending a clinic for sexual dysfunction (Schwartz *et al*, 1982), indicating an important but poorly understood role for prolactin in male sexual behaviour (Drago, 1984; Bancroft, 1988). Separate work suggests that hypothalamo-pituitary-gonadal axis (HPGA) dysfunction may be a feature of some paedophiles, who exhibit an elevated leutinising hormone (LH) response to leutinising-hormone releasing hormone (LHRH) when compared with non-paedophile paraphilics and controls (Gaffney & Berlin, 1984). Furthermore, men with Klinefelter's syndrome have similar LH release profiles (Smals *et al*, 1976), raised prolactin (Schiavi *et al*, 1978), and may also have an increased incidence of paedophilia (Mosier *et al*, 1960; Neilsen, 1972; Wakeling, 1972), although this is controversial (*Lancet*, 1988).

Case report

The patient, a 29-year-old storeman, was referred for a psychiatric court report after admitting to indecent assault over a four-year period against a girl who was six when the offences began in 1983. These took the form of kissing and fondling, after which he would masturbate, although with impaired potency and ejaculation. Sexual interest was only partly directed towards this girl, in that he also reported sexual fantasies involving adult women; he therefore satisfies the DSM-III-R criteria (American Psychiatric Association, 1987) for non-exclusive paedophilia.

He was educated in a remedial class, leaving school without qualifications and having a number of unskilled jobs. He is a shy, solitary man whose main interest is making models. His one adult sexual relationship, which started in 1981, lasted two years, ending before his offending began. Sexual difficulties were partly responsible for the end of the relationship, as reduced libido, erectile dysfunction, and ejaculatory failure had prevented successful intercourse. Previously, he had masturbated with full potency and ejaculation. In 1983 he also required circumcision for balanitis, at which time diabetes mellitus was diagnosed, and oral hypoglycaemics commenced. Past medical and psychiatric history, and family history, are unremarkable apart from maturity-onset diabetes in both parents.

At assessment he was noted to be obese with a somewhat high-pitched voice. There were no abnormal neurological signs or evidence of hypogonadism. Chromosomal analysis showed a normal male karyotype. An endocrine screen revealed a raised prolactin level (2398 mU/l, $n = 0–450$) and low testosterone level (10 nmol/l, $n = 14–42$). LH, follicle-stimulating hormone (FSH), thyroid function tests, liver function tests, electrolytes, and full blood count were all normal. He was not on any medication known to raise prolactin levels. Blood glucose averaged 6–9 mmol/l with a glycosylated haemoglobin of 9%. Investigation of hyperprolactinaemia included skull and pituitary X-rays, computerised tomography of the cranium, dexamethasone suppression test, and plasma and urinary cortisol, which were all normal. Neuropsychological testing demonstrated an IQ of 80 with a verbal IQ of 77 and a performance IQ of 91.

Although the time of onset of hyperprolactinaemia was unknown, it was considered that the raised prolactin was likely to have contributed to the offence in some way (see below), and that his prognosis in terms of reoffending would be good if his prolactin were normalised. After a short time on remand awaiting trial, he was sentenced to three years' probation with a condition of treatment. A period of psychiatric and endocrine in-patient care has been followed by out-patient management. Bromocriptine (2.5 mg t.d.s.) returned prolactin to normal within six weeks. On follow-up, prolactin levels have remained normal, although testosterone remains slightly low (11 nmol/l). Over this period there was a return of libido, erectile response, and ejaculation, and sexual fantasies were claimed to be solely towards adult women. However, this period also coincided with release from custody, and his reporting of sexual matters may have been influenced by this, as well as by a wish to be seen to respond to treatment. On follow-up, he continues to deny paedophile interests and is in full-time employment, but there has been little progress in terms of establishing adult sexual relationships.

Discussion

To our knowledge this is the first report of hyperprolactinaemia presenting in association with paedophilia, and as such complements the above findings relating this sexual disorder to other endocrine abnormalities. Clearly, no causal connection can be inferred from a single case, but several issues are raised.

Hyperprolactinaemia affects all three components of male sexual performance (libido, arousal, and ejaculation), but it is unclear which of these is a primary effect and which may be non-specific sequelae. Bancroft *et al* (1984) suggest that loss of libido is caused directly by hyperprolactinaemia, whereas the erectile dysfunction is a psychological reaction to the reduced sexual interest. Drago (1984), reviewing animal data, concludes that ejaculatory failure is more important, noting, however, that the effects of raised prolactin on male sexual function are complex and variable.

One explanation for our patient's offences might be, therefore, that the onset of hyperprolactinaemia precipitated overt sexual dysfunction and failure to maintain adult sexual relationships through both direct and indirect mechanisms. Sexual dysfunction, combined with his pre-morbid personality (characterised by shyness and social isolation) and limited intelligence, would have led him to perceive a sexual relationship with a child as less threatening. Increased anxiety and somatisation have been reported in hyperprolactinaemic men (Fava *et al*, 1982) and could have contributed to the sexual dysfunction, but these symptoms were not observed here. A more specific link between hyperprolactinaemia and paedophilia involving alterations in HPGA function, as described by Gaffney & Berlin (1984), cannot be ruled out.

In view of this case, together with the evidence indicating a connection of some kind between pituitary dysfunction, sexual problems, and paedophilia, an endocrine screen including prolactin should be considered as part of the assessment of paedophilia. To what extent the finding of a raised prolactin level should constitute a mitigating circumstance in terms of sentencing remains unclear. The 'medicalisation' of child sexual abusers is a contentious area, and the delineation of subgroups who have demonstrable organic or psychological problems which can be related to the offence may help identify boundaries of medical involvement.

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Neuroleptic Malignant Syndrome in a Case of Post-Partum Psychosis

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A 27-year-old woman with a post-partum psychosis developed NMS which proved difficult to diagnose because of the organic features of the presenting illness. Possible contributory factors to the development of NMS included exhaustion, a non-specific viral illness, and rapid loading with haloperidol.

The neuroleptic malignant syndrome (NMS) is a complication of neuroleptic use and is characterised by hyperpyrexia, muscle rigidity, and autonomic instability. There is disagreement about its incidence (Shalev & Munitz, 1986; Pope *et al*, 1986; Kellam, 1987). The combination of NMS and post-partum psychosis does not appear to have been described before. There has been discussion recently of mild and possibly atypical forms of NMS (Shalev & Munitz, 1986; Levinson & Simpson, 1986; Addonzio *et al*, 1986; Sullivan, 1987). The onset of NMS is well documented in our case and the full-blown syndrome was preceded by subtle and confusing changes which might well have gone unnoticed.

Case report

Mrs Z, aged 27, was referred to this unit one day post-partum because of confusion and difficult behaviour on the post-natal ward. Eight hours after delivery she had collapsed following micturition and had complained of chest pain. There was no history of chest pain before delivery. Electrocardiography and a chest X-ray were normal.

She had a history of a non-specific viral illness with myalgia and general malaise in the week before delivery and had been prescribed temazepam to help her sleep at night. There is no record of pyrexia at that time or of chest pain. Her previous obstetric history was unremarkable. Her delivery was normal.

There was no known relevant family history. She had no relevant previous medical history. She had a disturbed childhood and there is a history of mild antisocial personality traits and moodiness. She had been taken into care at 13 for stealing, promiscuous behaviour, and being beyond the control of her parents. She had taken overdoses. Her first marriage broke down within six months because of marital violence.

On initial psychiatric examination she was tired and anxious but readily reassured. She expressed concern about her new baby and at one point said that she thought the baby had not been born. She was orientated in time and space. She was treated with fluorazepam as a sedative, and was observed.

She became elated and deluded over the next 48 hours. She refused all contact with her baby daughter. Her level of consciousness fluctuated markedly from normal to stuporose. Her behaviour was worse at night. She misinterpreted sensory stimuli and was extremely distractible. When accessible she complained of persistent right-sided chest pain and tightness in her chest.

A provisional diagnosis of post-partum psychosis, probably manic, was made, but the rapid onset of her illness in association with her chest pain and history of recent viral illness raised serious concern about a possible organic basis for part or all of her problems. On the fourth day post-partum, to facilitate rapid investigation, she was sedated with chlorpromazine initially and then with intravenous and intramuscular haloperidol over the next seven days. In total she received 260 mg haloperidol (reaching a maximum of 80 mg daily) and 300 mg chlorpromazine. Despite the large doses of neuroleptics she remained agitated and extremely difficult to manage on the ward. A series of investigations were carried out including blood cultures, biochemical screening, full blood counts, urine cultures, HVS and lochial cultures, ECG and repeat chest X-rays. All results were normal. There was no leucocytosis.

On the seventh day post-partum an electroencephalograph (EEG) showed diffuse slow-wave activity. On the ninth day post-partum and five days after the introduction of neuroleptics she developed pyrexia, mild tachycardia, and labile blood pressure. On her 11th day post-partum a computerised tomography scan was normal. A lumbar puncture was performed and the cerebrospinal fluid was entirely normal. Routine biochemical and haematological screening remained normal.

The haloperidol was stopped and intravenous chlormethiazole was used to secure adequate sedation. Over the next week she received four sessions of electroconvulsive therapy (ECT). She improved steadily, particularly immediately after anaesthetic. She remained pyrexial with slight tachycardia and unstable blood pressure. Gardenerella was isolated from an HVS test and although this was not regarded as a likely cause of her clinical picture she was started on a course of metronidazole and cephradine.

On 18th day post-partum she developed stereotyped movements, rigidity, and posturing. A single dose of chlorpromazine (100 mg) was given (seven days after her last dose of haloperidol and 14 days after her last dose of chlorpromazine). Within four hours her pulse rate had risen to 150 per minute and she developed a pyrexia of 38.5°C per axilla. Her blood pressure became extremely labile. There was marked diaphoresis and sialorrhoea. Her respiratory rate became erratic and she had difficulty swallowing. She was noted to be very pallid. Over the next

24 hours she became increasingly catatonic, with extreme rigidity, hyper-reflexia, extensor plantars, stereotypy, and catalepsy. Her clinical signs fluctuated with great rapidity. For brief periods she appeared lucid but generally she was unresponsive. A working diagnosis of Gram-negative septicaemia was made and a further course of antibiotics was started. However, blood cultures were negative and a second lumbar puncture was normal. Alternative diagnoses were considered. A diagnosis of NMS was made and was supported by a raised serum creatinine phosphokinase (CPK) level of 1200 IU/l (normal range for women 24–170 IU/l).

She was treated with L-dopa (100 mg) combined with carbidopa (25 mg) (as Sinemet Plus) (one tablet q.d.s.) and dantrolene sodium (25 mg q.d.s.) for five days. L-dopa was then replaced with bromocriptine (10 mg t.d.s.). All other drugs were stopped. Her clinical state improved very slowly with gradual resolution of the autonomic instability, but she remained severely catatonic with marked catalepsy, stupor, and stereotypies. Her serum CPK level remained high, reaching a maximum of 1674 iu/l on the 20th day post-partum and only returning to normal values one month later. There was a slight elevation in her hepatic transaminases.

As she improved physically the drugs were reduced until on the 37th day post-partum both bromocriptine and dantrolene were withdrawn. She immediately developed a further low-grade pyrexia and her pulse and blood pressure became unstable. She settled on conservative management.

She remained catatonic. A repeat EEG showed slow-wave activity posteriorly. A second course of ECT was given, to which she responded quickly. By the seventh treatment she began to look after her infant under supervision. Immediately after anaesthetic she was noted to have an entirely normal affect and intact cognitive function.

Two months after admission she was discharged to community psychiatric care. Her mental state continued to improve and there is no objective evidence of any sequelae related to NMS.

Discussion

Post-partum psychosis and NMS are both rare conditions (Shalev & Munitz, 1986; Kellam, 1987; Kendell *et al*, 1987), although there is disagreement about the true incidence of NMS (Pope *et al*, 1986; Keck *et al*, 1987; Gelenberg *et al*, 1988). Their occurrence together has not been reported previously to our knowledge. A case of catatonia occurring two months post-partum was described by Morrant (1984) and NMS was considered as part of the differential diagnosis. Catatonia in the post-partum period in the absence of NMS is also described (Hanson & Brown, 1973).

In view of the reported association between NMS and exhaustion and debilitation (Itoh, 1977), patients suffering from post-partum psychosis might be expected to be at particular risk of NMS, and this may be worth investigating further.

As a consequence of observations and investigations instigated when she first presented, the episode of NMS is well documented in this case. The patient developed a low-grade pyrexia and a labile blood pressure five days after the first dose of neuroleptic (chlorpromazine) and during administration of haloperidol. These changes persisted after the cessation of neuroleptic therapy. She then developed a mild catatonic state with rigidity and hyper-reflexia about one week after the neuroleptics were withdrawn. We now believe that this was in fact a further sign of low-grade NMS.

This pattern of insidious development of NMS is well recognised (Addonzio *et al*, 1986). As pointed out by Shalev & Munitz (1986), it is the rate of loading that appears to correlate best with the development of NMS. There is some evidence that haloperidol in particular may be more hazardous when associated with rapid 'neuroleptisation' (Bollini *et al*, 1984; Keck *et al*, 1988) and can cause a high incidence of extrapyramidal side-effects and even death. The justification for such regimes is uncertain (Baldessarini *et al*, 1988). However, although the circumstances of this case led to rapid loading with haloperidol, the major life-threatening episode occurred following a single dose of chlorpromazine after seven days without any neuroleptics. We believe that a mild form of NMS began five days after starting neuroleptics and was then exacerbated by the reintroduction of chlorpromazine.

The organic features of post-partum psychosis are well recognised (Brockington *et al*, 1981), but, as in this case, may require further elucidation before the use of ECT. A particular diagnostic dilemma was raised by the presence of a low-grade pyrexia. Although infection and thrombo embolic phenomena are most often implicated, it should not be forgotten that post-partum psychosis alone may be associated with pyrexia, and that a mild fever and delirium were once felt to be characteristic features of such psychoses (Brockington *et al*, 1982). In this case the presenting symptoms post-partum suggested an embolic or infective aetiology and neuroleptics were used to obtain sufficient sedation to allow investigations to be carried out quickly. The pyrexia appeared nine days after the patient first developed the signs of a post-partum psychosis and was, as noted above, more closely associated with the use of neuroleptics and persisted after the neuroleptics were withdrawn. Thus the development of NMS caused organic signs which were then misinterpreted as further evidence for an organic basis to her illness. We would like to suggest that this situation may occur more often than is realised. The use of neuroleptics in organic psychoses or psychoses of uncertain aetiology requires awareness of this potential iatrogenic pitfall.

The treatment of NMS remains unsatisfactory. Pope *et al* (1986) stressed the need for vigilance not only because of the importance of stopping neuroleptics but also to allow the early use of appropriate therapeutic agents. Bromocriptine, dantrolene, carbidopa, and others have had unreliable effects and none have been shown to be of unequivocal benefit in all cases. Our case showed a gradual improvement over 21 days following the last administration of chlorpromazine. On withdrawal of bromocriptine she had pyrexia associated with a mild tachycardia and increase in blood pressure, and she became sweaty and pallid. These features suggest a possible recurrence of autonomic dysfunction associated with the withdrawal of the bromocriptine.

Some features of this case are similar to those described in cases of Stauder's lethal catatonia (Stauder 1934). The patient became catatonic immediately before the dose of chlorpromazine that precipitated florid NMS, and she remained catatonic for a prolonged period. Even in the absence of NMS, catatonia of acute onset remains a dangerous condition of uncertain aetiology (Ainsworth, 1987). The relationship between lethal catatonia, other catatonic syndromes, and NMS is unclear (Barnes *et al*, 1986) It may be that these conditions share a common neurobiochemical basis, possibly related to hypothalamic dysfunction (Horn *et al*, 1988). The apparent improvement after anaesthesia under the influence of barbiturates and benzodiazepines also occurs in lethal catatonia (Ainsworth, 1987) and may lead wrongly to the diagnosis of functional illness.

It is worth stressing that the marked fluctuation in clinical signs in this case caused considerable confusion (e.g. the absence of extensor plantar responses on some occasions) and led to differing interpretations of the significance of these signs with a tendency to underestimate the seriousness of the problem.

NMS remains a dangerous condition (Shalev & Munitz, 1986; Horn *et al*, 1988) and has been described in a variety of non-psychiatric settings. Death has resulted because of the difficulty of making the diagnosis in atypical situations (Allsop & Twigley, 1987). Only two of 31 cases referred from various sources to a neurological centre were correctly diagnosed at the time of referral (Destee *et al*, 1980). Conversely, the presence of fever in a psychotic patient is not often the result of NMS and organic causes must be excluded (Levinson & Simpson, 1986). As Kellam (1987) has pointed out, it is important to treat these patients in the appropriate place, usually the intensive-therapy unit. Conversely, it is our observation that increasing specialisation of nursing staff has led to difficulty in the management of patients who are both medically and psychiatrically seriously ill.

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Neuroleptic Malignant Syndrome and Psychotic Illness

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A typical case of NMS and its successful treatment with bromocriptine is described. The authors noticed an inverse relationship between the process of recovery from NMS and the pre-existing psychotic illness.

The neuroleptic malignant syndrome (NMS) is a rare and potentially fatal complication of antipsychotic medication manifesting as fever, rigidity, altered consciousness, and autonomic dysfunction (Levenson, 1985; Shalev & Munitz, 1986). Despite a considerable increase in its recognition (Adityanjee *et al*, 1988), the natural history of this iatrogenic condition remains controversial. It is only recently that studies on its long-term outcome have started surfacing (Levenson & Fisher, 1988; Susman & Addanozio, 1988). However, the relationship between the natural history of NMS and the pre-existing psychotic illness has not been explored adequately as yet.

Here we describe a typical case of NMS and its successful treatment with bromocriptine, a pure DA-2 receptor agonist. We also discuss the relationship between resolution of this syndrome and re-emergence of the original psychotic illness.

Case report

The patient, a 20-year-old, unmarried woman, presented in March 1986 with an 18-month history suggestive of schizophrenia. A diagnosis of catatonic schizophrenia was established as per ICD-9 guidelines (World Health Organization, 1978) and she was treated with 20 mg of trifluoperazine and 6 mg of trihexyphenidyl per day. After two weeks, the dose of trifluoperazine was increased to 30 mg per day. Subsequently she was prescribed promethazine (50 mg t.d.s.) for the next two weeks for extrapyramidal symptoms. Since rigidity and tremors persisted, all the drugs were stopped and she was put on chlorpromazine (200 mg per day). Next day she became restless and confused. She had fever and abnormal movement. She was brought to the emergency services; there was no history suggestive of any medical illness.

On examination, she was comatose. Her eyes were rolled up, and there was no stiffness in her neck. Pupils were mid-dilated and responded poorly to light. Fundi were normal bilaterally. Sialorrhoea was noticed at the angles of the mouth.

The patient was febrile (axillary temperature 42 °C), pulse was 100 per minute and regular, and blood pressure was 120/70 mmHg. There was no cyanosis, jaundice, or pedal oedema. The respiratory rate was 24 per minute. Auscultation of chest and heart did not reveal any abnormality. The abdomen was distended and the bowel sounds were poor.

Tone was increased in both upper and lower limbs. Tremors in both upper limbs were noticed. Tendon reflexes were poorly elicited all over. Plantars were down-going bilaterally. There were no meningeal signs. A provisional diagnosis of NMS was made, although differential diagnoses of cerebral malaria, acute encephalitis, and septicaemia were also considered. Her investigations revealed a haemoglobin level of 7.8 gm%, a total leucocyte count of 18 000, with a differential of 87% polys, 1% monocytes, erythrocyte sedimentation rate (ESR) of 60 mm. Peripheral smear for malarial parasite was negative. Random blood sugar was 225 mg%, blood urea 17 mg%, and sodium and potassium were 118 and 2.8 mEq/l respectively. Serum proteins were 6.8 g/l with an A:G ratio of 3.7:3.1. Serum bilirubin was normal. SGOT and SGPT were 41 and 4 IU respectively. Serum alkaline phosphatase was 11.5 IU. Serum creative phosphokinase (CPK) was raised (629 U/ml). An electrocardiograph was within normal limits. A chest X-ray revealed a parenchymal lesion in the left middle zone and right lower zone, and was interpreted as possibly due to aspiration pneumonia. A skull X-ray and computerised tomography of the head (plain) were also normal. Electroencephalography done a week later revealed a normal awake record.

The patient was started on antibiotics for aspiration pneumonia. Chlorpromazine was stopped and bromocriptine (5 mg t.d.s.) was started through a Ryle's tube. After four days bromocriptine was reduced to 2.5 mg t.d.s. as there was a gradual improvement. The same dose was continued for the next ten days. Her leucocyte count came down to 8800 on the second day of starting bromocriptine.

Five days after the admission her ESR was still raised (55 mm). Repeated chest X-ray revealed resolution of the parenchymal lesion. A muscle biopsy (deltoid) done two weeks after admission revealed a few necrotic fibres with phagocytes. There was no variation in the fibre size or any sign of inflammation. The pathologist's report considered the histological changes as non-specific.

Although the patient showed complete recovery from NMS and bromocriptine was gradually withdrawn over two weeks, she had to be started on electroconvulsive therapy (ECT) because of re-emergence of the original psychotic symptoms. She received six sessions of ECT over the next two weeks. Psychotic symptoms recovered completely and the patient was well for the next week without any treatment. However, there was a recurrence of psychotic symptoms. In the following week she developed insomnia, would spontaneously shout and cry without any reason, and became abusive and assaultive. She also manifested ideas of reference and ill-systematised persecutory delusions. She became socially withdrawn and was markedly negativistic. Five more sessions of ECT were administered, following which the symptoms remitted.

Three weeks after her admission her serum CPK was normal (28.5 U/ml). She was prescribed thioridazine (150 mg/day) and trihexyphenidyl (4 mg/day). No recurrence of NMS was observed and subsequently the patient was discharged.

Discussion

We successfully treated the NMS with bromocriptine (Mueller, 1985). The resolution of NMS in our patient, however, was followed by a re-emergence of the original psychotic illness, which required further treatment. Until now, not much attention has been focused on this problem in the literature.

There is a general consensus that the aetiology of NMS involves a sudden and massive blockade of the dopaminergic system (Hashimoto *et al*, 1984; Hermesh *et al*, 1985; Ansseau *et al*, 1986). On the other hand, a psychotic illness is characterised by a hyperdopaminergic state. Therefore, theoretically, the symptoms of psychotic illness should not be present during an episode of NMS. This is exactly what happened with our patient. However, owing to altered consciousness, a *sine qua non* for the diagnosis of NMS (Adityanjee *et al*, 1988), it is difficult to comment upon the severity of psychotic illness during an episode of NMS. Presumably the patient is often too ill to tell whether or not the psychotic symptoms have in fact cleared.

The process of recovery from the NMS episode would involve changes to neurotransmitter receptors which tend to undo the central dopaminergic blockade. This may eventually result in an overshoot phenomenon, that is, central dopaminergic overactivity that characterises a psychotic illness. Clinically, therefore, one would expect gradual worsening of psychotic symptoms as happened in the case illustrated.

It may be argued that the re-emergence of psychosis in our patient was probably due to bromocriptine, by virtue of its dopamine agonist activity (Levenson, 1985). Such exacerbation of psychosis, possibly due to the dopaminergic agonist action of bromocriptine, has not been observed commonly in doses used for NMS (Mueller, 1986). Moreover, it was prescribed for only two weeks. Such a short duration of treatment with low doses of bromocriptine, alone, does not explain the gradually progressive worsening of the original psychotic illness in our patient. Eventually, the patient required 11 ECT sessions for resolution of the psychosis.

We believe that the recovery from NMS in our patient was temporally associated with the re-establishment of the original disturbed neurochemical state, which manifested in the form of gradual worsening of psychotic symptoms. The case illustrates the natural history of recovery from NMS in a patient with psychotic illness.

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Anterior Tumour of the Corpus Callosum With Atypical Depression

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We report a patient with an anteriorly palced tumour of the corpus callosum presenting with primarily depressive symptoms, without any associated neurological abnormality. It is important to be alert to the possibility of an organic cause to depression.

In psychiatric practice, intracranial tumours are fortunately rare. Parry (1968) quotes a figure of 1 per 200 patients admitted to a psychiatric unit. Psychiatric symptoms, on the other hand, are a common presentation of intracranial tumours (Adeloye *et al*, 1969). Ironside & Guttmacher (1929) quote a large series which showed that 90% of corpus callosum tumours present with mental changes.

We report a middle-aged woman who presented with symptoms of an atypical depression, and who was found to have a tumour of the anterior portion of the corpus callosum.

Case report

A 55-year-old divorcee, who had had a depressive episode ten years previously, presented to the Department of Psychological Medicine, with a four-week history of becoming increasingly socially withdrawn. She had started to neglect her personal hygiene and housework, and had become very apathetic, spending most of her days in bed. She was increasingly uncommunicative, limiting her responses to 'yes' or 'no' or more frequently 'don't know'. Her family had commented that she had been depressed, but there was no diurnal variation in her mood or sleep disturbance, although there had been some loss of appetite and weight, as well as feelings of self-blame and hopelessness. On the ward her mood was labile, and she frequently adopted a rather silly, supercilious attitude. Neurological examination failed to show any neurological abnormality, but she was disorientated in time, although not in place nor in person. She found it difficult to concentrate, and had a marked memory deficit for recent events. Her memory for the remote past, however, was well preserved, as was her general knowledge. There was no evidence of dysphasia or any other cognitive disorder.

Computerised tomography of the brain revealed a large tumour of the corpus callosum invading both frontal lobes (Fig. 1). Burr-hole biopsy confirmed the histopathology to be a glioma.

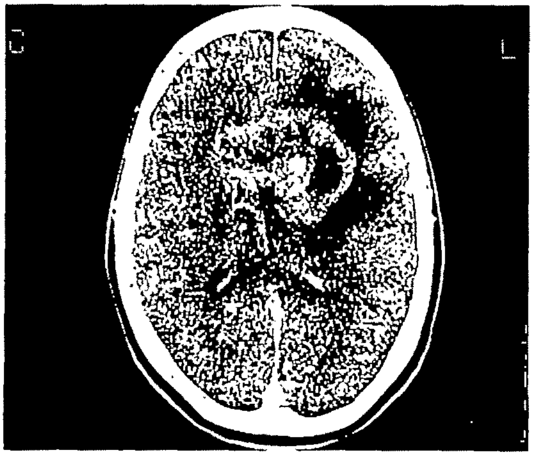

FIG. 1 The contrast-enhanced computerised tomography scan shows a mixed-density lesion between the frontal horns of the lateral ventricles, which are compressed. There is surrounding oedema.

Discussion

Alpers (1936) suggested that the diagnosis of corpus callosum tumours is possible directly on clinical grounds and that symptoms "pertaining to the mental sphere seem to be far more important than others". A large series was reported by Schlesinger (1950), who concluded that the anterior and posterior segments of the corpus callosum (in preference to the middle segment) are of greatest significance for the elaboration of mental symptoms. This finding was confirmed in a smaller series reported by Selecki (1964), who found that the anterior tumours in particular present early with mental symptoms, before progressing to dementia and long-tract signs, raised intracranial pressure being a late feature. He recorded a multitude of psychological symptoms as being components of the "fronto-callosal" syndrome. These included: loss of recent memory, indifference to environment and to emotion, slowness, change in personality, disorientation, confusion, dementia, apathy, drowsiness, torpor, stupor, coma, *Witzelsucht*, euphoria, puerility, delirium, and depression. In his five reported cases of fronto-callosal syndrome, disturbance of mood was not a prominent feature: only one had depression and this individual's history was complicated by chronic alcoholism; one other in the series had instability of mood and euphoria, but was also a heavy drinker.

Nasrallah & McChesney (1981) found significantly more depressive symptoms among five patients with corpus callosum tumours, compared with a group of patients with unilateral frontal or parietal tumours – one patient had a full spectrum of depressive symptoms, but this individual's tumour was located in the middle portion of the callosum, invading the parietal lobe. Those subjects with anteriorly placed tumours had less consistent depressive symptoms.

Our patient was typical in that she presented early with psychiatric symptoms, before the development of hard neurological symptoms and signs, but was unusual in that depressive symptoms were a prominent feature.

Early diagnosis of intracranial tumours is clearly desirable, but psychiatrists frequently see such patients with only psychological symptoms before the tumour has advanced to produce physical signs. Clearly then, careful assessment of mental state is of paramount importance, as well as awareness of the possibility of underlying brain tumours.

In the above case the question of organic brain syndrome was raised when the patient had short-term memory loss and was disorientated in time. The diagnosis was facilitated by a ready access to computerised tomography.

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Familial Manic–Depressive Illness with Deleted Short Arm of Chromosome 21: Coincidental or Causal?

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A 35-year-old Arab lady and her mother, both with bipolar manic–depressive illness and 46,XX,21p-(pcen→pter), are reported. The clinical significance of this association is considered.

The role of genetic factors in primary affective disorders has been implicated in family, twin, adoption, linkage, and biochemical studies (Murray & McGuffin, 1988; McKusick, 1988). Polymorphic variants of chromosome-21 short arms are common and are inherited as simple Mendelian traits; they are often found to be benign. In the present report manic–depressive illness (MDI) is described in an Arab lady and her mother associated with the 21p- variant.

Case report

BA is a 35-year-old woman, divorced with no children, who works as a clerk. She had several admissions to the Kuwait Psychological Medicine Hospital and to psychiatric hospitals in London, France, and the USA, for recurrent manic and depressive episodes during the last 18 years. She was assessed by a multispecialty team because of the associated menstrual disturbances, hirsutism, urinary urgency, and incontinence.

BA is the second of seven siblings delivered to second-cousin Arab parents and first-cousin grandparents. Her 57-year-old mother, who also has hirsutism and MDI since 1949, is under treatment. According to her mother, her milestones were normal. When ten years old, her parents noticed her introvert tendencies, with occasional outbursts of aggressive behaviour and hyperactivity under minor stress. She was not very successful academically. Her arranged marriage to a cousin, seven years ago, lasted only two months. She rejects remarriage and is now working as a clerk. Her performance is not very satisfactory. Her menarche started at 15 years, and was associated with excessive growth of facial and body hair. She had regular menstrual cycles until eight years ago. A gynecological and pelvic tomographic examination revealed enlarged ovaries with microcysts. Her hormonal profile was normal for serum oestradial, progesterone, testosterone, cortisol, and thyroid hormones. Chromosome analysis of peripheral blood cultures revealed 46,XX,21p- (p cen→p ter) chromosome complement confirmed by G, C and NOR banding techniques (micrographs available from author on request). Her mother showed an identical chromosome constitution.

The proband and her mother were assessed by the author. Both met ICD-9 criteria (World Health Organization, 1978) and Research Diagnostic Criteria (Endicott & Spitzer, 1979) for bipolar affective illness. None of the proband's six siblings suffers from major psychosis at the present time. Unfortunately, they refused to give blood for cytogenetic study.

Discussion

The proband and her mother both had MDI and a deleted short arm of chromosome 21. Unfortunately, cytogenetic investigations, which might have cast more light on the significance of this association, was refused by other family members. This association may be coincidental. Several factors have to be considered. (a) It is known that the sizes of satellites, stalks, and the short arm of both D- and G-group chromosomes vary. The frequency of p- in acrocentric chromosomes was estimated to be 0.5–1.0 per

1000 (Nielson *et al*, 1974). (b) There are a number of reports of heritable structural variations of the chromosome including the Gp- being associated within families with both normal and abnormal phenotypes (e.g. Ballantyne *et al*, 1976; Hsu *et al*, 1987). (c) Apparently, a complete absence of the short arm in acrocentric chromosomes is without any deleterious phenotypic effect, as demonstrated by people with balanced centric fusion: t(Dq, 21q) t(21q,22q) or t(21q,21q) (Rothere, 1981; Hsu *et al*, 1987). (d) There is no associated 21p- in the available reports dealing with chromosome variants and MDI (Say *et al*, 1977).

Recently, a number of reports discussed whether mania is really incompatible with Down's syndrome (DS) (e.g. McLaughlin, 1987; Cook & Levanthal, 1987, 1988; Singh, 1988). It is now well established that trisomy of only band 21q22 results in a DS phenotype identical to that caused by complete trisomy 21 (Rothere, 1981). The question is whether there is a true association between the genes on the long and short arms of chromosome 21 and MDI. It seems that a better understanding of this association is indicated to elucidate precisely the relationship between different genes and human behaviour. Certainly, the combination of the updated cytogenetic, biochemical, and DNA studies in psychiatric patients with either monosomy 21p or trisomy 21q22 or both will be beneficial.

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Chronic Psychosis in Turner's Syndrome

Case Report and a Review

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A 59-year-old woman with Turner's syndrome developed epilepsy, diabetes mellitus, chronic psychosis, and subsequently pre-senile dementia. This would endorse the view that psychosis in Turner's syndrome arises through brain damage.

It is estimated that Turner's syndrome (TS) occurs in only 0.01% of newborn girls (Evans, 1977), with a relatively poor rate of survival into adult life (Forssman, 1970). The rate of sex chromatin-negative karyotype among female psychotics is even less common – Akesson & Olanders (1969; quoted by Forssman, 1970) found only two cases among 6090 psychiatric patients.

We report a patient with TS who developed epilepsy, chronic psychosis diagnosed as schizophrenia, diabetes mellitus, and pre-senile dementia, along with other physical illnesses.

Case report

WQ was born in 1929, at full-term and without any medical complications. She weighed 8½ lb (4 kg), was bottle-fed, and had normal early development apart from a short stature. She has nine other siblings (including two pairs of twins), and to date no medical or psychiatric illnesses are reported in the family.

She is noted to have stopped growing at the age of nine years following tonsillectomy, and at age 19 to have remarked that she was 'a woman in a child's body'. She completed grammar school successfully and is described as having been good academically. As a result of her father's early death, her mother worked full-time while WQ looked after the younger members of the family. Before admission, she was an office worker for three or four years.

The patient was admitted to a mental hospital at 28 years of age following violent behaviour. She had developed epilepsy at age 15, and auditory hallucinations two years later. Early records indicate that although she was poorly investigated, anticonvulsant treatment was successful in reducing the frequency of her fits. However, her psychotic symptoms progressively worsened over the years. She believed that she heard voices from upstairs and from outside. At times she was convinced that they belonged to an aunt who spoke rude things about her. She also maintained that comments were made about her on television. Consequently, she would become quite agitated and throw things at the windows and the television. She felt that there were evil spirits in the house and refused to go upstairs into her bedroom. For some unknown reason, she started collecting handbags, and had a collection of 30 before she was brought into hospital. This pattern of psychosis continued for several years and led to her admission into hospital only when her aggressive behaviour worsened.

On admission, she was described as being disorientated, talking rubbish, incoherent at times, had echolalia, and showed abnormal behaviour. She had a blank expression, was considered to be aurally hallucinated, and frequently smiled and laughed without any apparent reason. Neurological examination was normal, with down-going plantars. She was diagnosed as having epilepsy with hebephrenic schizophrenia. Her grand-mal fits were controlled with phenytoin and phenobarbitone, but she remained chronically hallucinated, gesticulating at unseen tormentors and talking to her absent father, until she commenced treatment with trifluoperazine (15 mg o.d.) in 1963. Following this, she made notable improvement which lasted at least six years. Attempts at stopping her neuroleptics caused an exacerbation of her psychosis, with effective control on reinstatement. However, she continued to have infrequent fits and her mental state deteriorated despite various medications. She has had a number of fractures due to osteoporotic bones, and at the age of 51 she developed insulin-dependent diabetes mellitus.

She is now demented, with urinary and faecal incontinence, poorly orientated, lacking in registration and recall, and very poor in communication. Physical examination is as follows: height 4' 3" (1.29 m) short webbed neck, moderate degree of kyphoscoliosis, and slight cubitus valgus. There is mild generalised hypertonia, hyperextension of the interphalangeal and ankle joints, gait is unsteady, and tendon reflexes brisk bilaterally; plantar reflexes are extensors. Co-ordination could not be tested, and touch and pain sensations appear to be normal. She is presbyopic and hypermetropic, and has bilateral deafness. Fundi are normal. No cardiovascular abnormalities could be detected clinically. Other characteristic features such as poor development of secondary sexual characteristics and primary amenorrhoea are also present.

Routine blood tests were normal. Other investigations revealed normal chest and skull X-rays, an X-ray of her spine confirmed kyphoscoliosis, and computerised tomography showed generalised brain atrophy. Her chromosome pattern is karyotype 45 XO.

Discussion

There are very few reported cases of psychotic illnesses in patients with TS. Of 2946 studies relating to the syndrome, only seven have reported such an association. The earliest description is of a patient with Turner mosaicism and a family history of schizophrenia, who developed early-onset schizophrenia (Slater & Zilkha, 1961). An earlier report by Hampson *et al* (1955) found no cases of psychosis in their series of 11 patients, while Sabbath *et al* (1961), studying seven girls aged between 14 and 20, described a schizophreniform psychosis precipitated on one subject's engagement. Milcu *et al* (1964) reported a single case of schizophrenia in a sex-chromatin-negative patient, and Mellbin (1966) reported four patients, one of whom had a chronic organic psychosis and another epilepsy and a short-lived psychotic episode. In a detailed study of eight patients, Luria *et al* (1968) did not find a single case of major psychosis. Swanson *et al* (1973) described a brief psychotic reaction in a 33-year-old patient who responded to perphenazine, amitriptyline, and electroconvulsive therapy, and was free of symptoms at 12-month follow-up. A further report exists in the French literature, by Trapet *et al* (1981), describing psychotic episodes in monozygotic twins, one of whom had TS. Raboch *et al* (1985) compared 19 TS women with 18 women with pure ovarian dysgenesis and 50 gynaecological out-patients serving as controls. They concluded that two patients with pure ovarian dysgenesis and none with TS or in the control group suffered from serious mental disorder. In a cross-cultural study involving 111 girls with TS, Nielsen & Stradiot (1987) noted that 13% reported suffering from mental illness (unspecified forms), with only 1.8% having undergone psychological/psychiatric treatment.

A number of other studies have found a low incidence of TS among large psychiatric populations. Olanders (1967) observed that none of 1589 women in four mental asylums had absent Barr bodies, and also found a higher than average prevalence of 0.38% for double Barr bodies. Kaplan & Cotton (1968) surveyed 968 females diagnosed as schizophrenics for chromosomal aberrations and found only two cases of TS. A similar study by Anders *et al* (1968) failed to find any case of TS in 445 female schizophrenics. A larger survey by Akesson & Olanders (1969) of 3558 female psychiatric patients revealed only one patient with TS.

Thus psychotic reactions seem to be uncommon among TS patients. The reason for this is obscure. Extra X chromosomes have been regarded as predisposing to psychiatric illness (Forssman, 1970; Slater & Cowe, 1971); conversely, it is conceivable that the absence of an X chromosome would confer some immunity from major psychiatric disturbances. However, such a conclusion is difficult to draw from the few scattered cases of a very rare disorder. An important aetiological factor might be organic brain disease. Mellbin (1965) has reported five patients with TS, all of whom had electroencephalographic abnormalities.

Our own patient had temporal lobe epilepsy and generalised brain atrophy. Where such pathology is not so obvious, genetic loading might be an important factor, as in the cases reported by Slater & Zilkha (1961) and Trapet *et al* (1981). Hormonal deficiency is unlikely to contribute significantly to the low incidence of psychosis in such patients because it is almost invariably present, and also there were no striking differences between the groups studied by Raboch *et al* (1985).

In conclusion, this report describes a 59-year-old TS woman of previously normal intelligence who developed epilepsy, a schizophrenia-like illness, and subsequently pre-senile dementia, thus endorsing the view expressed by Mellbin (1966) that psychotic illnesses in these patients develop in the setting of brain damage.

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The Effects of Loss of Taste and Smell in a Case of Anorexia Nervosa and Bulimia Nervosa

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A woman with a mixed eating disorder is reported. Her disorder did not remit after a head injury which caused her to lose her sense of taste and smell.

A woman with a long history of eating disorder was admitted for assessment and treatment. Three years before referral she had sustained a head injury which impaired her sense of smell and taste, the results of which are explored.

Case report

A 43-year-old woman with a 20-year history of eating disorder, alcohol abuse, and obsessional–compulsive behaviour was referred to the psychiatric out-patient department and subsequently admitted. Her height was 162 cm and she weighed 49 kg at referral. She had been amenorrheoic for five years.

The patient had been overweight as a child and weighed 77 kg during her early teenage years. As a university student she reduced her weight to 57 kg by dieting. At 20 years she abandoned her studies, and started to drink heavily. Over the subsequent five years her weight fell from 56 kg to 37 kg. At 25 years her eating pattern changed and she began to avoid all food before 10 p.m., when she would eat a large carbohydrate-rich meal prepared in a ritualised manner and accompanied by large quantities of alcohol. She also started bingeing frequently at other times on bread, cakes, cream, and sweets. She avoided self-induced vomiting, but consumed large quantities of laxatives. Her weight remained low and she became amenorrhoeic, resulting in two admissions to psychiatric hospitals for the treatment of her eating disorder. This resulted in a temporary improvement only. At 32 years of age she became depressed and was treated with antidepressants with some benefit, and continued to work as a successful executive.

Three years before referral she was robbed and seriously assaulted in the street. She was struck on the head with an iron bar and sustained a fractured occipital bone with loss of consciousness for 48 hours. She suffered complete anosmia and her sense of taste remained sensitive only to very sweet or salty stimuli, findings which were confirmed by two neurologists and, at the time of admission to this unit, by an ENT surgeon.

Following her head injury the patient's diet underwent a dramatic change. The texture of food became of paramount importance. Her main meal consisted of more than 1.5 kg of crunchy muesli as well as fruit and biscuits. She consumed at least 50 pints of milk each week. In addition, she regularly binged on cream cakes, chocolate, and sweets. She unsuccessfully attempted to give food flavour by adding salt and rich combinations from the 50 or more spices which she kept in stock. Yoghurt was flavoured with a tablespoon of saccharin tablets, coffee and tea were highly concentrated, and her preferred alcoholic drinks were fizzy beers and wines. She did not feel hungry or thirsty during the day and felt no satiety after eating. Her obsessional–compulsive behaviour, including hand-washing and preparation of food, also became more ritualised and time consuming. Food had to be arranged on her bed and bedside table in a fixed way, and she consumed the food in a rigid sequence. She avoided food before noon.

On examination she was thin, highly aroused, anxious, and emotionally labile. She agreed that she was underweight and suggested a healthy weight for herself of 53 kg. However, she became distressed when advised to gain weight. There was no evidence of memory impairment or other cognitive abnormalities.

The patient scored 99 on the Eating Attitudes Test (mean for normals is 15, and for anorectics is 58) (Garner & Garfinkel, 1979). On the Maudsley Obsessional–Compulsive Inventory her overall score was 17, which is typical of obsessional–compulsive patients (Hogson & Rachman, 1977). A computerised tomography scan showed mild cerebral atrophy and an electroencephalogram was normal.

The patient was admitted to a general psychiatric ward with the aim of helping her to establish a normal eating pattern, to gain weight, and to tackle her obsessional–compulsive beaviour. The two principal components of the treatment programme consisted of a closely supervised behavioural regime and skilled nursing care. Breakfast and lunch were gradually introduced, accompanied by restriction on night-time binge eating. Ritualised food sorting and preparation was also eliminated and finally all night-time eating was stopped. Targeted compulsive behaviour was prevented in a step-by-step fashion, and alternative non-ritualistic behaviour was encouraged.. The patient had difficulty in adhering to this programme. When the night eating was completely stopped her weight fell rapidly as a result of eating meagre meals. When she reached 44.5 kg it was decided to transfer her to a specialised eating disorders unit, with closely supervised nursing care (Russell, 1984). Her weight rose to 51 kg after four months in hospital, and after a further three weeks, during which she was free to supervise her own diet, she was discharged.

She has been followed up in the out-patient department on a regular basis for 12 months. After discharge she initially lost weight, going down to 38.7 kg after three months, but then recommenced a pattern of alternating starvation and nocturnal binge eating, with a resulting 12 kg increase in weight. During this period of follow-up the patient has reported frequent episodes of sleep walking, during which bingeing occasionally occurs. She has successfully abstained from laxative and alcohol abuse.

Discussion

Abnormalities of taste and smell are not uncommon sequelae of head injuries, blows to the occipital region being the most likely to give rise to deficits (Schechter & Henkin, 1974). The resulting loss of pleasure in eating can be distressing. Nevertheless, this unusual case suggests that just as an inability to see oneself does not protect against anorexia nervosa (Yager *et al*, 1986), the inability to taste food does not offer protection against binge eating.

From 20 years until 25 years this patient had a history of anorexia nervosa. This was followed by a stage, lasting until the time of her presentation, which was characterised by symptoms of anorexia nervosa (calorie restriction, fear of weight gain, low weight and amenorrhoea) and bulimia nervosa (frequent binge eating and laxative abuse accompanied by weight gain). This overlap of symptoms occurs in a substantial minority of patients, and in order to recognise this heterogeneous clinical picture, the most appropriate diagnosis is that of a mixed eating disorder, i.e. combined anorexia nervosa and bulimia nervosa (Russell, 1989).

Post-traumatic anosmia and ageusia frequently lead to changes in diet. In a series of 29 patients with post-traumatic abnormalities of smell and taste (Schechter & Henkin, 1974), 16 had noticeably increased the addition of salt, and six had added extra sugar to their diet. Nine lost weight. The patient reported here did not lose weight after head injury, but she gave a graphic account of her desperate attempts to stimulate her sense of taste. Interestingly, the content of binges rather than their frequency or calorific content was altered following the head injury. Although the taste of food was important to the patient, evidently it did not play an important role in regulation of binge eating.

Although the taste of food has been shown to contribute to satiety (Le Magen, 1985), no specific abnormalities of taste have been demonstrated in patients with eating disorders. However, normal-weight bulimics and underweight anorectics have been shown to have a preference for sweeter stimuli which does not alter with acute changes in body weight (Drenowski *et al*, 1987). It has also been demonstrated that anorectics on a low-calorie diet have a heightened sucrose taste sensitivity in comparison with anorectics on a refeeding regime and normal-weight controls (Lacey *et al*, 1977). Since this patient remained both anorectic and bulimic despite almost total loss of taste, it would appear that such an increased sensitivity is unlikely to be of major importance in the maintenance of an established eating disorder.

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Unresolved Grief Presenting with Features of a Negative Therapeutic Reaction

ANNE M. NIGHTINGALE

A 44-year-old depressed widow in psychodynamic psychotherapy suffered repeated relapses of symptoms following improvement. This was seen as a negative therapeutic reaction.

A patient is described whose five-year history of depression started following the death of her husband and appeared to represent an unresolved grief reaction. In psychodynamic psychotherapy she showed a pattern of gaining relief from her depression in one session followed by a worsening of the intensity of her symptoms in the next. This had been characteristic of her symptom pattern throughout her illness. This was viewed as a 'negative therapeutic reaction' in which an unconscious sense of guilt or need for punishment operated to prevent relief from suffering. Some psychoanalytic theories regarding mourning are discussed in relation to this case.

Case report

Mrs A, a 44-year-old widow, was referred for assessment for psychotherapy by her general practitioner in November 1987. She was a deeply religious woman in full-time work as a medical receptionist who gave a five-year history of low mood, episodes of weeping when alone, and disturbed sleep mostly as a result of frightening dreams. There was no history of appetite nor weight disturbance nor diurnal mood variation, but for one month before her referral the intensity of her symptoms had greatly increased, she was experiencing considerable difficulty in concentrating, and her feelings of intense distress had become so acute and persistent that she feared she would be unable to cope. She found night-time particularly difficult, troubled as she was by recurrent dreams of being alone and detached from other people, and she characteristically awoke in the morning with an overwhelming sense of aloneness coupled with a physical sensation of being desperately ill. She had contemplated suicide, although she felt guilty about this in view of her religious convictions. She was also complaining of an increased frequency of migraine headaches, about three per week.

The symptoms had been present since her husband's death five years previously but had become much more intense following the departure of her sister for North America following a three-month visit.

The younger of the two sisters, Mrs A had grown up locally in a family which she did not describe as close. Her father was apparently a quiet and unassuming man who seemed to the patient unable to stand up to her mother who could at times be rather vitriolic. At age 20 the patient married a man whom she knew to be paraparetic following an accident. She acknowledged that this was in part to get away from her family and also felt that her husband showed her the kind of care she had never had at home. She admired his zest for life and courage in the face of his handicap. However, soon after she married she discovered that her husband had lied to her about the extent of his handicap and that he was in fact impotent. She was greatly distressed by her inability therefore to have children, and felt that his attitude towards her over this was humiliating to her. Eventually the couple adopted two children, the younger of whom, Elizabeth, was later found to be severely mentally and physically handicapped. Mrs A found looking after Elizabeth very difficult as the child needed constant care but could give nothing back. When Elizabeth was three years old the couple arranged to put her into a residential institution on medical advice. However, Mrs A subsequently felt extremely guilty about this and six months later developed symptoms of anxiety associated with a fear of "going berserk" and harming someone. At that time she was admitted briefly to a psychiatric hospital.

Mr A developed renal failure as a complication of his spinal injury and died after a prolonged illness. Mrs A felt guilty about the way in which she thought that she withdrew from him emotionally before his death, and at her presentation she said she was still grieving for him.

It seemed that Mrs A was suffering from a depression of moderate severity which appeared to represent an unresolved grief reaction. She received 15 sessions of weekly psychodynamic psychotherapy using a brief focal psychotherapeutic approach along the lines described by Malan (1979). In therapy she explored her feeling of aloneness which she traced back to her childhood experiences with her mother. She realised that her husband had been the only person who was able to dispel this and that his death had allowed the return of this aching sense of emptiness from her childhood. In acknowledging this she realised the extent of her depression and the severity of her depressed feelings over the previous five years. She seemed more able to tolerate her pain and allowed herself to grieve freely for several weeks.

At the same time she explored some of her own angry and aggressive feelings over which she had always felt very guilty. In particular these related to Elizabeth and to Mr A. She was inclined to see such feelings as evil and was alarmed to consider that there might be a side to herself which was identified with the unpleasant side of her mother.

However, she gradually became more tolerant of this part of herself and began to see how she had coped with these feelings by splitting them off from her normal competent and capable social self. Thus her daytime self contained all her strengths and her night-time self contained all her fear, her aloneness and her anger which were revealed in her dreams particularly. The frequency of her migraine attacks diminished, and she began to feel more at peace with herself.

However, it was striking that on each occasion when she reported an easing of her symptoms the following session would reveal that her depression had returned in full force. When this was pointed out to her she said that she herself had noticed that whenever she became aware of an improvement this seemed to be immediately followed by a return of the 'black depression' as if 'all that seemed better gets reduced to no value'. The therapist interpreted to her the possibility that her new found feelings of happiness might feel like a betrayal of her husband, as if in finding some happiness without him she were triumphing over him and his memory, and her guilt over this sense of betrayal kept returning her to her suffering and grief. Mrs A replied with a memory of which she had not spoken previously. Apparently the day after she and her husband had taken Elizabeth to the residential home a priest came to visit them. It seemed that he had come expecting to comfort them in their grief but in fact found the two of them in formal dress about to leave the house to go out for dinner. She recalled clearly the expression on his face and remembered her impression that he had judged her severely for what appeared to be the ease with which she had got over her daughter's departure. She readily connected that experience with later ones around the time of her husband's death, and following this her symptoms gradually improved.

Mrs A's general practitioner reported that ten months after therapy her symptoms had not recurred, and she was apparently making plans to remarry.

Discussion

When Freud (1917) compared mourning with melancholia he said both were characterised by 'a profoundly painful dejection, cessation of interest in the outside world, loss of the capacity to love and inhibition of all activity' but in addition in melancholia he said there was a lowering of self-regard 'to a degree that finds utterance in self-reproaches and self-reviling and culminates in a delusional expectation of punishment'. Freud pointed out that 'In mourning it is the world which has become poor and empty, in melancholia it is the ego itself', and he put forward the hypothesis that the lowering of self-regard in melancholia with its attendant self-criticism represents not a set of complaints against the ego, but 'plaints' directed against the loved person to whom an attachment previously existed. A part of the ego, by a process of identification with the lost object, has subsequently become the target of these attacks; to quote Freud's famous phrase 'the shadow of the object falls upon the ego'. By implication then, Freud's view in *Mourning and Melancholia* (1917) was that although in melancholia a process of internalisation of an ambivalently loved object had occurred, this was not the case in normal mourning, the work of which consisted in a process of repeated episodes of reality testing whereby the loved object is found no longer to exist and all the libido invested in attachments to that object is withdrawn.

Abraham (1924) however, suggested that internalisation of the loved object also occurred in the work of normal mourning and Klein (1940) elaborated this further. She suggested:

> "The poignancy of the actual loss of a loved person is, in my view, greatly increased by the mourner's unconscious phantasies of having lost his internal 'good' objects as well. He then feels that his internal 'bad' objects predominate and his inner world is in danger of disruption. . . . He not only takes into himself the person whom he has lost but also reinstates his internalised 'good' objects (ultimately his loved parents) who became part of his inner world from the earliest stages of his development onwards. These too are felt to have 'gone under', to be destroyed, whenever the loss of a loved person is experienced."

The work of mourning, then, in Klein's view consists not only of the slow and painful process of reality testing but also of rebuilding 'with anguish the inner world, which is felt to be in danger of deteriorating and collapsing'. Klein draws particular attention to the role of triumph in impeding the work of mourning through interfering with the process of reparation towards the loved object. The reparative drive arises from guilt and despair at the loss of the loved object and represents the wish to restore and re-create the loved object internally. She suggests that triumph over the lost object forms part of the normal process of mourning but where it is particularly strong it may interfere so greatly with the act of reparation (carried out by thoughts, activities or sublimations) that:

> "objects which were to be restored turn again into persecutors . . . When hatred of the lost loved object in its various manifestations gets the upper hand in the mourner, this not only turns the loved lost person into a persecutor but shakes the mourner's belief in his good inner objects as well."

This lady had strongly ambivalent feelings towards her husband, and on each occasion that she experienced a release from her mourning her unconcious sense of triumph over him led to the return of her guilt over her hostile feelings towards him. In addition, her husband then became for her a persecutory and retaliatory figure whom she could not internalise as a good object as she needed to do to complete the work of her mourning. In this way she was 'tied' to her grief for him and showed the clinical picture of a negative therapeutic reaction (Sandler *et al*, 1970), that is 'the worsening of the patient's condition following some encouraging experience'. This case illustrates the psychological process underlying one example of a negative therapeutic reaction. Interpretation of this led to the presentation of further confirmatory material and to the relief of her symptoms.

The negative therapeutic reaction is of interest clinically and theoretically but has received little attention in the psychiatric literature. Recent research into recovery from depressive illness has highlighted persistent or recurrent depression in a significant minority of such patients (Keller *et al*, 1986). It is possible to speculate that negative therapeutic reaction may be relatively widespread and not confined to patients undergoing psychological treatments.

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Contents: The myth of hysteria as illness/Comparison of diazepam and buspirone/ASC and water intoxication/Better to be depressed in the sun/Self-harm and depressive disorder/Brain white-matter lesions and psychosis/Trichotillomania/Failure to convulse with ECT/Spontaneous orgasms – an explanation?/Pseudodementia/Beclomethasone mania

The myth of hysteria as illness

SIR: If a restaurant served perfectly good food but the sign outside declared that it was all poisoned, even the hungriest customer would keep away. If the poison sign was removed, crowds would pack in. I wish to welcome and emphasise the equally dramatic implications of Birtchnell's reconsideration (*Journal*, September 1989, **155**, 425–429) of *The Myth of Mental Illness* (Szasz, 1961).

Like Dr Birtchnell, I have always felt it should go under a more modest and accurate title; my choice would be *The Myth of Hysteria as Illness*. In the book (this one, anyway), Szasz only minimally suggests that the argument applies across all that we call mental illness. As a private practitioner of psychoanalysis, he rightly kept to his area of expertise – normal and neurotic, not psychotic. Admittedly, the infamous title does represent what he has since argued, and the book would certainly not have sold so massively to a general public under a modest title.

By an interesting coincidence, the same issue of the *Journal* contains Taylor's excellent exploration of 'Hysteria, belief and magic' (*Journal*, September 1989, **155**, 391–398) in which he repeats and expands on this same 'point of view' – that psychiatrists strangely mirror the hysteric by wishing to label and treat hysteria as if it were a disease when by definition there is none (Taylor, 1986). Taylor (1982) has also developed a more discriminating framework than our medically rooted diagnostic system, which treats everything as if it belonged in the realm of 'bioscience'.

Dr Birtchnell refers to other authors interested in the realm of 'personal conduct' and 'interpersonal' theory and diagnosis. One quite concrete form of interpersonal assessment in ordinary psychiatric interviews (Child, 1983*a*) has supported the hypothesis that hysterical personality (if not hysteria) is best considered in interpersonal terms, and that such labels are attached to patients who are 'disagreeable' in general, and specifically in the patterns of looking and speech in the psychiatric interview (Child, 1983*b*). So Dr Taylor's ideas may be considered more substantial than just a 'point of view'.

The surprising conclusion about Szasz's infamous book is that the very psychiatrists (organicists) who believe it to be so poisonous by its outward sign are likely to find most food for thought inside, for they too hold that hysterics are not truly ill and so are not worthy of the attention they seek from psychiatrists. Unfortunately, therefore, the organicists' potential sympathy for Szasz's basic thesis does not characteristically extend to the patients themselves, and consequently organicists may not really be interested in a model of human conduct such as Szasz sets out in the book. So they may choose another 'restaurant' to eat in. But without its poisonous 'sign', at least they will respect, recommend and possibly even sample 'Café Szasz' rather than avoid and slander it.

The late R. D. Laing got his signs right and his recipes exotic but brilliant. His anti-establishmentarianism gained him the same popularity and infamy as Szasz. If he had wished to be taken more seriously by psychiatrists, I would have given him tactical advice in the same vein as renaming Szasz's book. Strategically, Laing should first have emphasised his ideas as applying to normal or neurotic functioning, not to psychotic – and certainly not as a cause of psychosis, however valid that suggestion might also be.

There are other instances of mistaken 'public relations' in this area of psychiatry, all the more astonishing because the mistakes have been made by the very people who are claiming superior skill in communication and interpersonal strategy. Bettelheim (1983) showed how Freud's translators converted ordinary German words into strange technical terminology in English, forever annexing much of the easily comprehensible 'soul' in his work. However, unlike Szasz, Laing and the others, Freud did want to establish a biological basis for psychoanalysis.

Poor tactics are evident even in the banners under which proponents of the various 'psychotherapies' stand. The term 'therapy' is obviously meant to match physical 'therapies', thereby obtaining equal status with the likes of organic psychiatry, surgery, and medicine in lecture programmes and health services. Equal status there should certainly be. But unfortunately, 'therapy' also contains all the other implications that go with a 'bioscientific' approach. However little surgeons and physicians know about psychiatry and psychotherapy, they do know that they are operating in quite a different realm, and they instinctively resist.

So the psychotherapies are hoist by their own petard. For example, it is much easier with physical therapies to tell whether the patient has taken the doctor's advice or not. Of course, psychotherapy is more than just advice-giving, but a lot of it is about 'resistance' of various kinds. In the (inevitable) absence of concrete description or 'markers' of what happens in the interactions and process of psychotherapy, mere attendance for appointments may be equated with 100% compliance with treatment. Attending appointments on its own would never be a sufficient criterion for assessing the efficacy of a physical treatment. Again, the sign outside the restaurant has promoted decades of serious misunderstanding – and it is *not* really the outsiders' fault.

With this belated clarification, I commend fellow psychiatrists who have previously and understandably been repelled from entering some fine restaurants in our quarter of town, to shut their eyes to the misleading (and now immovable) signs outside, and feast within!

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Comparison of diazepam and buspirone

SIR: In the past year British psychiatrists have received concentrated advertising designed to persuade them to prescribe buspirone for anxiety. It has been hinted that buspirone is less likely to lead to dependence than diazepam. Murphy *et al* (*Journal*, April 1989, **154**, 529–534) continue this theme.

Dr Murphy *et al* had four active treatment groups, each with only ten patients completing. There was no placebo group. The striking thing about their displayed results is that patients in all groups got better with the passage of time and the receiving of attention. At the end of 14 weeks, whether patients had had no active treatment for the past eight weeks or no active treatment for the past two weeks, as groups they were all much improved and did not differ from one another. Nor, one may suppose, would they have differed from a placebo group.

While anxiety levels were still initially high, and before time could have brought resolution, diazepam was significantly superior to buspirone in anxiety relief. There was also clear evidence of withdrawal effects after diazepam.

Dr Murphy *et al* have demonstrated again that diazepam is effective and that a drug effective against anxiety will lead to eventual withdrawal symptoms. Buspirone, not being noticeably effective, did not lead to noticeable withdrawal effects. Lack of potency of buspirone is no recommendation for its prescription.

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ASC and water intoxication

SIR: I would like to thank and clarify the interesting points raised by Cooney (*Journal*, August 1989, **155**, 266) regarding our case report (Lee *et al*, *Journal*, April 1989, **154**, 556–558). Dr Cooney expressed surprise at our suggestion that we were not aware of previous reports of the use of water to induce an altered state of consciousness (ASC), for three reasons: (a) many of his patients with excessive fluid intake presented as 'drunk'; (b) case 1 in Singh *et al* (1985) turned to excessive water drinking because it made him feel slightly drunk; and (c) Ripley *et al* (1989) remarked that mild overhydration may be experienced as pleasurable, leading to further polydipsia.

The first observation is based on Dr Cooney's unpublished personal experience, and should not therefore lead to surprise at our report. As for the second reason, Singh *et al* (1985) did not elaborate on or discuss the brief sentence noted above, and actually stated in the beginning of their paper that "water does not alter perception" (this speaks against an ASC which characteristically causes perceptual distortions and body image change (Ludwig, 1966)). Besides, it was not clear whether depression (the patient's diagnosis) with an accompanying self-harming motive or an enjoyable ASC was the primary aetiological factor. It will take a meticulous reader to spot that sentence and think about it in the perspective of ASC. Incidentally, we have quoted even earlier and more likely mentions of ASC ("a feeling of unreality" and hysterical fugue in patient 2 (Barlow & De Wardener, 1959)) in our paper, but again ASC was not specifically discussed. A more recent review does not include ASC or allied factors in its discussion of possible aetiological factors in polydipsia (Illowsky & Kirch, 1988). Hence, we consider that it is still worthwhile to highlight ASC in our case report. Concerning the third reason, Ripley *et al*'s paper was published several months after our report was submitted and accepted for publication, and aims to show an association (they suggested both genetic and psychological reasons) between alcohol abuse and water intoxication in schizophrenic male patients. No specific discussion was made on ASC, which in my opinion may provide a valuable link between drunkenness from alcohol abuse and "pleasurable polydipsia" as hinted at by the author. Incidentally, a pleasurable experience, such as eating good food, may or may not constitute an ASC as it is usually described – Ludwig (1966) listed nine general characteristics. Viewing compulsive water drinking as "maladaptive ASC" (Ludwig, 1966) also carries treatment implications because, if verified, it will be possible to replace this potentially dangerous habit by methods of developing "adaptive ASC", as by self-hypnosis or Qigong, a popular Chinese breathing and physical exercise.

There is also some misunderstanding about water drinking in traditional Chinese medicine. A large amount of cool water does achieve a mildly 'cooling' effect, but an intake of 20 litres/day is exceptional, apparently because of the physical discomfort that ensues. Besides, most Chinese would prefer to take a smaller amount of a more potent 'cold' remedy (e.g. bitter tea or melon) rather than water (Koo, 1984), so that our patient's adverse complications are still very unusual. Cigarette smoking and the list of aetiological factors cited by Dr Cooney are all irrelevant to our case. Finally, I would be interested to learn, with regard to the "many patients with excess fluid intake who present as drunk" to Dr Cooney, what kinds of patients they are and whether it is feasible to investigate their drunkenness using an ASC scale.

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Better to be depressed in the sun

SIR: Further to the correspondence following the papers by Lee & Murray (*Journal*, December 1988, **153**, 741–751) and Kiloh *et al* (*Journal*, December 1988, **153**, 752–757), may I be permitted to suggest an alternative explanation to the apparent difference in outcome between London and Sydney depressives? It is now accepted that phototherapy is an effective treatment for the seasonal affective subgroup of endogenous depression. It is highly likely that representatives of this subgroup were included in both the London and Sydney cohorts. With, I gather, the exception of this year, the climatic differences between foggy London and sunny Sydney are well accepted. Might not therefore the Sydney group have unwittingly been practising autophototherapy as they disported on Bondi Beach and its environs?

Rather than suggest the drastic step of emigration to the Antipodes, might not Drs Lee & Murray advise their depressive patients to take a long sea voyage around the West Indies, thus proving what our Victorian forebears knew well?

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Self-harm and depressive disorder

SIR: Ennis *et al* (*Journal*, January 1989, **154**, 41–47) found a 31% point prevalence of major depressive episode (MDE) in their sample using DSM–III criteria. We conducted a similar study at Reims Hospital's Emergency Unit with 113 deliberate self-harm patients consulting a psychiatrist (Théret *et al*, 1988). A 58% point prevalence of MDE was found using the Structured Clinical Interview for DSM–III–R (SCID).

As discrepant results may arise from different methods, we would like to discuss some points. The DSM–III–R criteria for MDE are known to be more stringent than those of DSM–III, so the discrepancy of results cannot be explained by the use of different classifications. In our study the cases of self-harm were restricted to drug self-poisonings, but it is known that the latter account for approximately 90% of the former. The sample of Ennis *et al*'s study might not be representative of the patients consulting in psychiatry after a deliberate self-harm at Toronto Hospital, since only 23% (71 of 251) of the patients admitted for that cause at the Emergency Department entered the study. The inter-rater diagnostic reliability was low ($\chi = 0.445$) despite the use of a checklist containing the DSM–III criteria for MDE. A standardised diagnostic assessment tool would have been more appropriate. The results are thus of less practical value. Finally, an astonishing statement by the authors is that attempted suicide and parasuicide are synonymous terms. Such an assimilation could lead to a confusion in the definitions. Kreitman's definition of parasuicide (Dyer & Kreitman, 1984) does not take suicidal intent into account, so that parasuicidal (or deliberate non-fatal self-harm) people constitute a much broader group than suicide attempters.

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Brain white-matter lesions and psychosis

SIR: The phenomenon of late-adult onset psychosis has long posed one of the more vexing problems in neuropsychiatric practice and research. Past investigative efforts have focused on the relationship of this aetiologically heterogeneous syndrome to cognitive disability, structural brain disease, and perceptual, in particular auditory, impairment. Miller *et al* (1989) have made a substantial advance in our understanding of late-life psychosis via their recent discovery of extensive sub-frontal white matter lesions by magnetic resonance imaging in almost 20% of the sample studied. The precise mechanism by which the demonstrated subcortical frontal damage might induce a psychotic process remains open to speculation. Like Miller *et al*, we have been struck by the coincidence of white matter disease and psychotic symptomatology. Other examples include metachromatic leukodystrophy, vitamin B_{12} deficiency, and certain cases of multiple sclerosis. We are writing to draw attention to a hypothesis we recently put forward in an attempt to explain the induction of psychiatric disturbance by white matter damage (Merriam *et al*, 1989). In brief, we have suggested that deep frontal white-matter lesions may compromise the integrity of certain corticofugal fibres originating in prefrontal cortex which serve to inhibit the mesolimbic dopaminergic system. Disinhibition of this system is in turn speculated to manifest as a psychotic process. There is substantial evidence that damage to the prefrontal cortical cell bodies from which these fibres originate causes pathological excitation of mesolimbic transmission (Pycock *et al*, 1980). Weinberger (1987) has speculated that idiopathic schizophrenia is the result of a similar process which, although congenital, does not manifest until the brain's dopaminergic systems mature and come 'on line'. We suggest that frontal white matter lesions may induce an acquired version of the same process and thereby surface as a psychotic disturbance.

Our hypothesis posits a causal cascade whereby acquired regional brain dysfunction induces a derangement of neurotransmitter systems traversing those regions; this neurochemical alteration in turn manifests itself as a psychosyndrome which is a phenocopy of an idiopathic psychiatric disorder. The hypothesis put forward to explain the onset of major depression after cerebral infarction posits a similar sequential relationship. Robinson *et al* (1984) have demonstrated that the incidence of post-stroke depressive episodes bears a direct relationship to damage to a particular brain region, in this case the left frontal lobe. Such lesions are thought to compromise ascending adrenergic pathways and thereby induce a depressive syndrome. We submit that the identification of these sorts of sequential causal relationships, whereby central nervous system lesions evoke neurochemical alterations which in turn evoke behavioural abnormalities, represents a promising avenue for the further understanding of brain-behaviour relationships.

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Trichotillomania

SIR: In their interesting report of a female victim of incest with trichotillomania, Singh & Maguire (*Journal*, July 1989, **155**, 108–109) conclude that sexual conflicts must always be considered when assessing trichotillomania. I would like to add two points to this conclusion.

Firstly, the authors do not mention the presence or absence of trichophagia (hair eating) in their patient. This is essential to ascertain, because of the well-recognised complication of trichobezoar. Mere enquiry is insufficient, as evidenced by Grant *et al* (1979), who reported a trichobezoar occurring when trichophagia was denied. At operation there was incontrovertible evidence of recent hair ingestion. Enquiry into gastrointestinal symptoms, physical examination and further investigations where relevant should be considered when assessing trichotillomania.

Second is the well-worn question of the role of iron deficiency in the picas in general. This has been debated for decades, and there are many anecdotal reports of a dramatic response to iron therapy (e.g. Coleman *et al*, 1981). However, a controlled study in the mentally handicapped (Bicknell, 1975) did not support the conclusions of earlier investigators (e.g. MacDonald & Marshall, 1964) that iron deficiency is aetiologic. McGhee (1980) reported trichotillomania and trichophagia in two children with iron deficiency anemia whose behaviour ceased when serum haemoglobin was restored to normal levels. One had a trichobezoar, one did not. Whatever the relationship – whether primary or secondary – the occurrence of iron deficiency in conjunction with trichophagia is sufficiently well documented to indicate that a full blood count and serum iron estimation should be considered when assessing trichotillomania.

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Failure to convulse with ECT

SIR: Complete inability to convulse in ECT has occasionally been reported (Sharpe & Andrew, 1988). This issue has long been controversial (Freeman, 1988; Pippard & Russel, 1988). Electrical parameters such as electrode placement, stimulus waveform, duration of pulse train and amount of energy delivered have been discussed as possible contributing factors. In clinical practice, the most widespread ECT devices use sine-wave stimulus waveforms (often modified). Pippard & Russel (1988), referring to such instruments, argued that the effective amount of energy delivered is probably too low to induce seizure and a satisfactory clinical response, suggesting that a constant current stimulus of 275–325 mC lasting about 3.25 ms at pulse rate of 50–60 Hz could overcome the problems of a minority of patients with high seizure thresholds. Freeman (1988) agreed, proposing the use of an ECT device which is able to deliver 2000 mC at maximum setting for high threshold patients.

We report a clinical observation, with a modern brief-pulse, constant current device (Thymatron, Somatics) on a cohort of 115 patients (age range 18–78) for which ECT was prescribed by their consultant. Energy delivered ranged from 75.6 to 302.4 mC, with a duration of pulse train that ranged from 0.6

to 2.4 s at pulse rate of 70 Hz. Impedance was controlled through the Thymatron impedance meter.

There were only seven missed seizures out of 557 treatments (1.2%), while no patients showed a complete inability to convulse during each ECT session. One patient only showed more than one missed seizure for the session (two out of four). The energy we delivered is considerably lower than that reported by Freeman and Pippard & Russel, and this discrepancy could be explained in terms of the critical electric parameter of the stimulus waveform. The superiority of the brief-pulse waveform compared with the sine wave form in terms of efficacy has been well documented in a number of controlled studies (Weaver *et al*, 1977). In fact, a square wave delivers all of its energy above the threshold, whereas the sine wave delivers substantial amounts of below-threshold energy (Maxwell, 1968). The consequence of this is that all the energy delivered (without dispersion) is valid to induce seizure.

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Spontaneous orgasms – an explanation?

SIR: Al-Sheikhli (*Journal*, August 1989, **155**, 269–270) reported a case of spontaneous orgasms in a 45-year-old lady in the absence of gynaecological, hormonal, or overt psychological disturbances and asked for an explanation for the phenomenon. The next step in management should be a careful search for organic brain disease. Lishman (1978) cites a case where a hemangioma of the medial surface of the sensory cortex caused similar experiences localised to the contralateral side of the vagina (Erickson, 1945). This lady's symptoms occur in a transient, episodic, recurrent fashion, which is the basic format of most epileptic disorders. Skull X-ray, an EEG and a computerised tomography scan could help to rule out structural pathology causing secondary electrical changes. A trial of antiepileptic medication seems worthwhile, even in the presence of an apparently normal EEG. This basic 'organic work-up' is essential before any psychological avenues are explored.

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Pseudodementia

SIR: Howells & Beats (*Journal*, June 1989, **154**, 872–876) describe an intriguing case with partial recovery, to which we should like to add our own experience.

Recently, for the first time in the 10-year history of our unit, we have admitted several unusual cases of 'pseudodementia'. These were four females with florid illnesses, unknown to each other, and admitted at different times. Two were married, one had been living with a common law husband, and one was recently widowed. Three were Canadian born, and one was a West Indian immigrant. Ages ranged from 70 to 80 years. Previous history consisted of a discrete episode of depression, 30 years earlier, in one case and several admissions over 20 years to mental hospitals in other countries, in another. The patients had received ECT. Otherwise there was no history of psychiatric disorder, or drug or alcohol abuse. Histories of the present illness ranged from six months to three years.

The cases presented with bizarre behaviour, varying from frenetic activity and screaming to withdrawal and somnolence. The behaviour varied both between cases and over time. Central to the mental states were dysphoric mood, anxiety, confusion, and Ganser responses. However, only one case approached the level of major affective disorder. All did badly, initially, on tests of cognition and function. On our unit, which acts as a tertiary referral centre, examinations by psychiatry, internal medicine, neurology, neuropsychology, EEG and brain imaging did not show irreversible dementia. Sodium amytal interview proved valuable in one case with the person temporarily reverting to normal; it was contraindicated in two cases on medical grounds, and one patient became extravagant but remained confused. In hospital the four patients were assumed to have an atypical depression and were placed a monoamine oxidase inhibitor (MAOI) drug for several months. Two of these patients made a total recovery in hospital, with one remaining well and the other relapsing after discharge; one remained calmer, but confused, on the medication; and the last made no response. Following discharge one remained well, and the other three required chronic care; one to the point where she needed total nursing care as though she suffered from an irreversible dementia.

What we call this syndrome is a moot point. Hysteria or Briquet's syndrome is a complex matter and readily misdiagnosed (Slater, 1961, 1965). It is often thought to be associated with being young or unsophisticated to the point that Brody (1985), in a discussion of our ageing society and changing illness patterns, wrote that " 'conversion hysteria', one of Freud's most frequent diagnoses, seems to have vanished". Kiloh (1961), in emphasising the need for vigilance with depressive pseudodementia, took pains to distinguish it from the hysterical variety. Whitlock (1982) cautioned that the Ganser syndrome of approximate answers may be wrongly equated with a hysterical form, since Ganser did not think that his patients feigned illness. Ganser symptoms are much more common than the syndrome and occur across psychiatry. Lastly, Bulbena & Berrios (1986), in a thorough survey of the topic, questioned the existence of hysterical pseudodementia.

In our group there seemed to be an interaction between anxiety, dysphoric mood and possibly personality and marital relationships. Merely calling the cases depression, or depressive pseudodementia, did not do justice to the clinical picture. The two married ladies did seem dependent. However, they found their husbands controlling, an opinion shared by the ward staff. Neither of these women improved lastingly. Improvements took place in the recently widowed and the previously common law wife. The widow was ambivalent about her marriage, which had not been happy. She continues to do well after one year on phenelzine.

In summary, our four cases are a mixed bunch. The best result was achieved with the lady with the shortest history, who seemed to benefit from phenelzine and widowhood. Sodium amytal interview was not given in her case due to medical contraindications, but proved useful in the other successful MAOI-treated, albeit relapsing, case.

The group exhibited a kind of pseudodementia. This is based on negative findings on investigation and some response to sodium amytal interview and an MAOI drug. The ultimate prognosis is uncertain but generally, in the short term, is grim. The explanation is unclear but the role of unsatisfactory marriages, even lengthy ones, has to be noted. All geriatric psychiatry units need to be aware of these cases and the need for a standard protocol in their assessment and treatment.

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Beclomethasone mania

SIR: In his study of mania in the elderly, Stone (*Journal*, August 1989, **155**, 220–224) suggests that cerebral organic impairment will be increasingly recognised in a multifactorial aetiology. The following case of an unusual drug reaction supports this view.

Case Report: In November 1988 a 69-year-old man had a two-month manic illness. This followed a course of oral prednisolone (reducing from 20 mg/day) for obstructive airways disease. There was no family or previous psychiatric history, and a diagnosis of steroid-induced mania was made. He recovered two months after the onset.

In April 1989 he again developed mania three weeks after starting Beconase (beclomethasone dipropionate) nasal spray for allergic rhinitis. It is suspected that he took twice the prescribed dose. On admission to hospital he was restless and disinhibited. His speech was pressurised and cirumstantial. He described his mood as "being on top of the world". He also had vivid complex visual hallucinations of animals, and auditory hallucinations of friends talking to him. He was disorientated with poor short and long-term memory function.

His Beconase spray was stopped. He improved over a 6-week period while being treated with haloperidol, and was discharged home. Three months after presentation he was well, other than some slight reduction in short-term memory.

The only abnormal physical investigation was a Computerised tomography brain scan, which showed diffuse cerebral atrophy and a lacuna infarct adjacent to the head of the right caudate nucleus.

Beclomethasone dipropionate is a potent corticosteroid used for the topical treatment of seasonal and perennial rhinitis. It is approximately ten times more potent at a cellular level than prednisolone. The recommended dose is 400 microgrammes per day (two 50 microgramme doses in each nostril twice a day). At this dose its efficacy is similar to 5–10 mg/day of oral prednisolone. Systemic effects do not occur with recommended dosages (Mygind, 1982). At higher doses adrenal suppression has been demonstrated (Harris *et al*, 1974).

Psychiatric effects have not before been reported. This case suggests that mania can follow higher than recommended doses and emphasises the susceptibility of the organically impaired elderly patient to mania.

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A HUNDRED YEARS AGO

Lunatics in Irish workhouses

The total number maintained during the past year amounted to 4,083, the idiot class being composed of 1,903 individuals, 360 of them being epileptic, and the demented of 2,180, of whom 389 were epileptic. On the whole, they are considerately treated, and regarded as special objects of benevolence, while, as infirm or sick, their dietary, which is discretionary with the physicians, is above that given to the ordinary workhouse inmate. The Inspectors of Lunatic Asylums have recommended the advisability of providing in each district one or more poorhouses, so arranged as to accommodate hopeless, aged, and tranquil cases, thereby disembarrassing asylums to a certain extent, and affording means of admitting into them curable and urgent cases at all times, without incurring the erection of new, or the enlargement of existing, asylums, and avoiding an uncalled for expense in their maintenance. If, at the annual rate of £12 or £14 per head, certain classes of the insane can, without any detriment to them, be supported in one institution, there is no reasonable cause why in another their capitation maintenance should amount to £22.

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Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

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Book Reviews

Editor: Sidney Crown

Narcissism and Intimacy: Love and Marriage in an Age of Confusion. By Marion F. Solomon. New York and London: W. W. Norton and Co. 1989. 217 pp. £16.95 (hb).

"It has been a basic assumption of this book that solid marital relationships are of such value that we need to develop a theory of dynamic marital therapy as a specific discipline with a focus on realising the potential of a secure, intimate relationship for emotional growth."

This penultimate sentence in Solomon's book rightly stakes a claim for marital psychotherapy alongside individual, family, and group therapy. More often than not, at least in Britain, marital psychotherapy is viewed as a by-product or a constituent of family therapy, and not recognised as a specific treatment of choice in its own right.

In the first part of her book, Solomon looks at the nature of marital relationships with particular reference to narcissism, which is to be understood as "a continuum from archaic to mature forms". Romantic love, normal idealisation, and parenting, she says, involve elements of mature narcissism, and will offer sustenance to a marital relationship. More primitive narcissistic states produce feelings of deep anxiety and vulnerability, emptiness and inner loneliness, and will put unbearable unconscious pressure on the partner to mend these deep wounds.

The author also refers to the unconscious choice partners make when they choose each other, motivated by "the unconscious hope of repeating what was good, and repairing what felt bad or lacking in earlier primary interactions". She goes on to emphasise the point: "Marriages are made not in heaven but in the earliest dynamic interactions between parent and child, which are repeatedly re-enacted in adult relationships".

In the second part of the book, Solomon turns to clinical practice, and writes that marital psychotherapists need to work with the transference and countertransference that develops "in the relational space between husband, wife and therapist". She makes the very important point that in marital psychotherapy the therapist has to work with the couple as a unit rather than with the individuals, because for the marital psychotherapist the marriage is the patient.

What this reviewer found frustrating was that in drawing on both systemic and psychoanalytic concepts, the gains achieved from this breadth of approach were outweighed by the losses of subtlety and depth. For instance, the author writes that "we cannot speak of an individual without recognising that the self exists only in context". Quite right. What she fails to point out, however, is that the *internal world*, peopled by very powerful and important objects and images, provides just as influential a context as does the external world. There is also a lack of emphasis that what the marital psychotherapist needs to look out for is not only the maternal and paternal transferences (among others): most crucial is the transference to the parental *couple*. It will be this internal image, unconsciously shared by the marital couple, which will play a major role in determining the nature of their relationship. For this reason, there is a strong argument for marital psychotherapy to be conducted by cotherapists whose therapeutic partnership will both invite the shared-couple transference as well as provide the arena within which it can be experienced, made conscious, understood, and used therapeutically.

Finally, the concepts of projective and introjective identification are central to an understanding of marital interaction, and to the clinical practice of marital psychotherapy. The former gets little more than a brief reference, the latter none at all.

With these qualifications, the book is a rich introduction to the complex task of thinking about and working clinically with couple relationships.

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Radical Constructionism – Rethinking the Dynamics of Development. By Melvin Feffer. New York: New York University Press. 1988. 224 pp. $44.00.

Professor Feffer's book is predominantly, although not exclusively, about the developmental relationship between causally determined behaviour and teleologically governed functioning; he recognises the inherent conflict between the two and attempts to integrate them into a coherent and harmonious synthesis. To achieve this he rejects the Cartesian dichotomy of object and subject, which he finds implicit in the Freudian model of development, and instead he draws on other ideas of cognitive functioning, particularly Piagetian 'schemata' and the 'patterns rather than parts' concepts of Gestalt psychology, in order to painstakingly erect his own theory of 'radical constructionism' as an explanation and even redefinition of the processes, essentially cognitive, which, he proposes, are involved in personality development. His positions are probably more logically and philosophically correct than those of Freud, with whose views Feffer chooses to compare his own, but then he has the benefit of an additional century of epistemological development and scientific observation. I find it sad and frustrating when today's thinkers treat the great man's pronouncements as static end-states, while *he* never considered anything he proposed as either definitive or final.

The book consists of one long, meticulously argued theoretical position, yet in contrast to the theoretical positions upon which it draws, those of Freud, Goldstein, Piaget, and of Gestalt psychology, it fails to persuade about its clinical relevance; in fact, it does not even attempt to. The practising professional will not find the bait of usefulness at the end of the intellectual hook and, since the book is not easy to read and is quite pricey, its appeal will remain limited to theoreticians of psychophilosophy.

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The Passionate Technique: Strategic Psychodrama with Individuals, Families and Groups. By ANTHONY WILLIAMS. London: Tavistock/Routledge. 1989. 238 pp. £15.00 (pb), £30.00 (hb).

The author provides an overview of basic psychodrama, and represents it in terms of systems theory and strategic therapy. He deals with transference, contracting, interviewing-in-role, family-of-origin practice, and the use of action methods as part of family therapy. Lively case examples and reports of full psychodramas carry the reader step by step towards a systems-sound structure in which spontaneity can flourish.

The author brings to the work of Moreno a strong theoretical background which creates a firm discipline of technique without disturbing the emotional content of the process. He posits that the aim of strategic therapy is to attempt to solve a problem which the client presents, and that the problem needs to be defined both in concrete terms and in terms of a relationship with others. He is concerned with interpersonal conflicts rather than intrapersonal ones, since the former is the concrete expression of the latter. He sees the individuals as living their role, or many roles, in relation to their "social atom". The Role is the Self. The basic problem is one of displaced or distorted love and loyalty within the individual's social atom.

The discipline required of the group leader is emphasised in relation to the problems which can occur when psychodrama is allowed merely to allow the individual to reinforce the negative or to become reliant on the sessions for the expression of the negative (the therapy of the moment). The client, imprisoned in a role, may well be wanting the therapist to enable him or her to play that role more effectively rather than to change. The discipline also calls for a much greater identification of the real problem at the interview stage, as well as an emphasis on the time which should be devoted to the warming-up process.

This is a vital book for all who work in psychodrama, as well as for all those whose work with individuals includes the process of Gestalt or guided imagery.

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Children's Phantasies. By OTTO WEININGER. London: Karnac Books. 1989. 314 pp. £14.95.

Otto Weininger, a Canadian, has worked as researcher, therapist, professor, and head of a school for emotionally disturbed children. His basic premise is that unconscious individual children's fantasies underlie all human activities. This book describes individual children's fantasies through therapeutic experience with parents, teachers, therapists, and other aspects of external reality. The stages of development of fantasies that lead to normal functioning are outlined in topics such as splitting of good and bad experiences, aggression and love, anxiety and independence, feeling, thought and creativity, and psychotherapy with children.

Susan Isaac's books, including *Social Development in Young Children,* are the underpinning for Weininger's book. However, because of his informal, narrative style, *Children's Phantasies* is more approachable for students beginning their work in a medical or school setting. The theoretical framework presupposes sympathy with psychoanalytic thinking; however, critics of such thinking are free to utilise the sensitive observations as raw data from which to form their own hypotheses and treatment techniques. Indeed, the vignettes, even when one disagrees with some of the theory, stimulate such questions as why adolescents dress in mother's clothes, or underachieve, as well as questions about how normal children can be helped with 'temporary psychotic episodes', mother's miscarriage, a sense of badness and regressive withdrawal. Parents might be interested in Weininger's ideas about assisting destructive children in finding ways of making reparation and enabling them to restore their essential belief in their own 'goodness' as children.

By suggesting everything is known, our own theoretical frameworks sometimes blind us to the possibility of seeing fresh approaches to helping children find the path to healthy development. The section on thinking, reassessing and decision-making challenges us to rework some of our own theoretical frameworks. For those who find didactic textbooks a bore, this book provides a pleasurable, enriching way of thinking about children.

The play psychotherapy section unfortunately lacks some of the emotional and theoretical richness of the rest of the book. One of the greatest gifts a therapist can give to a child is a depth of feeling and space in one's mind for thinking about the child's feelings. Weinberger's suggestion that the therapist use various concrete expressions of his or her goodness such as marshmallows and gifts seem to diminish rather than enhance the significance of the therapist's presence. For this reason I do not find myself in agreement with his notions of gifts. Likewise, the recommended short notice for ending therapy does not do justice to the importance of having and losing the relationship with the therapist. For greater understanding of child psychotherapy the reader might find it more useful to examine the British psychotherapeutic methods described in *The Child Psychotherapist* (edited by Dilys Daws and Mary Boston, Wildwood, London, 1977).

I would recommend this as a basic text for all courses discussing communicating with children in a school, clinic, or hospital setting. Students will find the book interesting when thinking about such questions as why children demand to have so many toys and in particular just the toy with which another child is playing, and why a child is unable to symbolise, play and defend himself from aggression. I would also recommend Weininger's book to clinicians, who will be enriched through thinking about the detailed, vivid descriptions of crises and ways of helping the children in the natural settings of home and school.

JEANNE MAGAGNA, *Principal Child Psychotherapist, Department of Psychological Medicine, Hospital for Sick Children, Great Ormond Street, London WC1*

Adultery – An Analysis of Love and Betrayal. By ANNETTE LAWSON. Oxford: Basil Blackwell. 1988. 440 pp. £13.95.

Adultery is an adventure and a myth. It attracts people constantly with the promise of dangerous passion. Lawson intends to look at the phenomenon as the underside, the breach of marriage and an undercover institution with its own walls. Adultery is seen as being firmly tied to marital breakdown, and it can be a sordid, mudane, meaningless, or empty affair.

The whole subject of adultery poses interesting moral, social, and religious dilemmas. The myth of love equalling marriage and the expectations of a one-to-one relationship contribute to the phenomenon of adultery. With ever-increasing divore rates, Lawson asserts that there will come a time when marriages will not last long enough for the partners to have adulterous relationships. She incorporates the myths of 'romantic marriage' and 'me' into her understanding of adultery. The sample was collected from newspaper and magazine readers. Some of the conclusions drawn from the study are obvious; for example, that the 1960s and 1970s were the most liberal times, when most respondents had their first liaisons; that the later the duration of onset, the lesser the number of affairs; that a significant minority met through work and a majority found happiness in it; and that more women were likely to feel guilty than men.

The author poses some interesting questions but her attempt at answering these is lost in the mists of descriptive details of histories of respondents. It would have been helpful to have included the methodology of the study in the main text of the book, rather than relegating it to the appendix, since the results from the study crop up from time to time in the main text.

Adultery remains an interesting social phenomenon (or is it to be seen as social deviance?), and this book may provide some flashes of insight into it, but not a total insight.

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Childhood Epilepsies: Neuropsychological, Psychosocial and Intervention Aspects. Edited by BRUCE P. HERMANN and MICHAEL SEIDENBERG. Chichester: John Wiley and Sons. 1989. 264 pp. £26.95.

This is a book of which the series editor, Professor Michael Rutter, can be justly proud. It is a valuable addition to the many recent publications on epilepsy and concentrates on areas in which others have been limited, namely the neuropsychological and psychosocial aspects. Here there are also sections on such clinical matters as classification and information processing in petit mal epilepsy. It is not an easy read, but it repays careful study.

The majority of the chapters consist of excellent literature reviews on, for example, cognitive function and academic achievement; then the authors present original research to fill in the notable gaps in current knowledge. There are problems matching patients with epilepsy to normal controls, as in the section on anticonvulsant effects. This is not least because epileptic discharge *per se*, during intelligence testing, may produce a low estimate of IQ and then the patient is matched with a less able normal control. The chapters often unexpectedly present numerical data on such matters as the effect of epilepsy on the family as well as on behaviour and social competence. Perhaps the importance of the poor self-esteem of many patients could be more emphasised, along with the useful place of sport in helping to overcome some of the problems. There is, however, an excellent section on vocational and psychosocial intervention for youths, presenting the American experience.

It might be felt that the volume is too slanted towards the USA, with 18 of the 21 contributors from that side of the Atlantic, but clearly their services, at least in some areas of the country, are much better organised than in the UK. The book therefore presents views which if studied carefully could improve overall management. It might seem trite, but the emphasis on seizure control itself is one of the single most important aspects for the production of a satisfactory psychological and social functioning, hence rightly the question of compliance receives considerable attention. Some more recent work on adults, with microprocessor counters in the caps of bottles, has shown just how poor compliance is, especially when drug regimes are complex, with multiple daily dosings, and the same appears to be the case in children.

The book is well produced, so the reviewer need not have been alarmed by the misprint in the second paragraph of the preface! The various chapters add up to a very informative volume that demands the attention of all those who care for the individual patient. It also clearly indicates the direction for future research.

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Sexual Trauma in Children and Adolescents: Dynamics and Treatment. By Diana Sullivan Everstein and Louis Everstein. New York: Brunner/Mazel. 1989. 224 pp. $25.

The authors of this book are psychologists working in the emergency treatment centre, Palo Alto, California, and this volume is a sequel to their earlier book, *People in Crisis* (New York: Brunner/Mazel, 1983).

The book is well organised; there is an introductory chapter on the problem of molestation, further chapters on assessment of trauma and treatment, and a final chapter on legal and ethical considerations.

The glossary of terms is useful, but the authors' definition of sexual abuse, sexual assault, molestation, etc. are idiosyncratic, sexual assault being defined as any degree of penetration, which does not take into account the assaultative quality of non-penetrator abuse.

The book itself is a bit of a curate's egg, with sections which are coherent and sensible alternating with statements which seem to be based on opinion rather than fact. For instance, the authors make clear statements about Freud's avoidance of the reality of child sexual abuse, and the subsequent avoidance of the subject by clinicians, leading on to a discussion of the role of the adult abuser in seducing the child. However, at the same time, sweeping statements are made about normal sexual orientation in adults, for example, "Although incestuous thoughts, fantasies and impulses are part of the normal developmental process of every person, society bans even discussion of the subject" (p. 89). Interesting though this statement may be, it is not substantiated by research, nor is the dogmatic statement that "The incest taboo ... draws its strength from sound biological, sociological and psychological reasons" – there is in fact a lack of consensus between anthropologists about the basis for the so-called incest taboo.

The book is weakest in relation to assessment issues, and far more convincing in relation to treatment. This may relate to the structural model of understanding incest proposed by the authors, which seems simplistic and is based on the concept of separate disturbed individuals in the family acting out pre-existing 'scripts' on the basis of past experience. The family itself is not viewed as a systemic entity, although incestuous family systems are mentioned. Since the authors do not have a concept of a sick family, but rather of sick individuals, they are able to recommend that "It is not always necessary or wise to recommend removal of a child from the home, or to advocate breaking up of the family system" (p. 113), which, while true for a substantial number of child sexual abuse cases, does not take account of sick family systems, which pose a risk to children even when the alleged perpetrator has been removed.

The assumption here is that if a disturbed adult can be helped, then all will be well: there is no understanding of pre-existing dysfunction within the family, and the need to address this specifically.

Similarly, the chapter on assessing children and talking to victims about abuse is sympathetically written, and contains much which is helpful to clinicians, but also contains contentious elements. The recent American experience, in certain states, of banning the use of anatomically correct dolls in interviews with abuse victims is reflected in the chapter, with the authors stating that using the dolls at all "enhances the likelihood that a child will be asked 'leading' questions by the examiner" (p. 24). No evidence is put forward to support this statement, and, although clinicians would be advised to use anatomically correct dolls with caution, and only after specific training, it is possible to interview children in this way, using an unstructured free play session, with few, if any, leading questions, towards the end of the interview.

The issue of leading questions itself is dealt with under the heading "Approaching the subject of incest" (p. 112) where a suggested approach is as follows: "As you know, relationships between fathers and daughters can become very close. Some of the things that you told me gave me the feeling – and you may stop me if I am wrong, because I am not always right – that something might have happened between you and your dad that hurt you or frightened you or confused you." Elsewhere, the authors, in common with others in this field, strongly warn against the use of leading questions. By legal standards, however, the example above is leading and suggestive, and would be subject to severe criticism in court, were the interview to be video-recorded or transcribed.

In the chapter on legal and ethical considerations, Richard Gregg, a lawyer, states that "Information storage in psychotherapy should be approached as discreetly as one would handle a loaded weapon" (p. 179). The possibility of excluding information from clinical notes, if it is to be read aloud in court, or if the clinician feels it to be harmful to the child or parents, is commended, in order to maintain confidentiality. Many of these considerations are now irrelevant under the current child protection procedures operating in Britain, whereby all such information, in relation to child abuse, may be shared with professional colleagues, and where, particularly, videotapes of interviews with children are now expected by courts, so that all statements, leading or otherwise, are available for scrutiny. The American context in which assessment is described in the book may therefore be misleading for British clinicians.

Treatment issues are sensitively and confidently covered by the authors, with a helpful chapter on the boy victim, which points out that after abuse less emotional damage may be reported in boys, because of the current macho, USA culture, which pressures men into "emotional damage control" with trivialisation of traumatic experiences. There is no mention of group work for child victims, and much of the treatment seems to involve initial psychological testing, followed by individual psychotherapy conducted along Freudian lines.

In conclusion, this interesting book, written from an American viewpoint, with the inconsistencies described above, would best be avoided by practitioners new to the field of child sexual abuse, and might be useful, in part, to more experienced practitioners.

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Recent Developments in Adolescent Psychiatry. Edited by GEORGE L. K. HSU and MICHAEL HERSEN. Chichester: John Wiley & Sons. 1989. 436 pp. £30.65.

This book intends to present "the most up-to-date information on treating all the disorders most commonly associated with adolescents". It is designed for "mental health practitioners and clinicians, researchers, professors and students". The book is divided into three parts: the first considers historical context, developmental aspects, diagnostic issues, and modes of evaluation; the second part covers the management of crisis, suicide, and legal issues; and the third is a series of chapters on specific disorders. The 17 chapters are by different authors, the whole book being edited by two well-known academic clinicians from the University of Pittsburgh School of Medicine. The editors point out that psychoanalytic viewpoints still tend to dominate the field of adolescent psychiatry and that they aim to fill a gap in the extant literature by drawing on empirical data. They favour a clinical approach which begins with the establishment of diagnosis followed by the development of a treatment plan, and have "therefore adopted the diagnostic scheme of the DSM-III-R throughout the book".

The different contributions vary in their interest and usefulness. With 17 chapters each is necessarily relatively short, and it could not be expected that there would be in-depth comprehensive coverage of the field. For example, there is throughout relatively little emphasis on aetiology, and specific psychotherapeutic treatments, including behavioural treatments, are usually dealt with much more briefly than psychopharmacology. It is unsatisfactory that in treatment for conduct disorders drug therapy gets four times as much space as behaviour therapy, and that under the heading of schizophrenia, family treatments to influence expressed emotion are alluded to somewhat dismissively. In contrast to the stated aims, the first two chapters on historical context and developmental issues repeatedly use psychoanalytic terminology and a dogmatic style. Certain chapters, such as those on diagnosis, crisis management, anxiety and affective disorders, work relatively well, as does that on suicide, although this does not apparently aim to explore self-injurious behaviour fully. For British readers the chapter on the law is interesting but not so specifically applicable, while that on attention deficit disorder makes no comment on transatlantic differences. However, the latter does refer to Farrington's and Loeber's work which is strangely absent in the list of references pertaining to the chapter on conduct disorders. Personality and developmental disorders are not separately covered, and for some reason the only reference to Tourette's syndrome occurs in the chapter on mental retardation, which has almost nothing on pervasive developmental disorders.

This book cannot be wholeheartedly recommended, because of its very uneven quality. It would probably have been improved by more strenuous editorial action to encourage contributors to focus on particular recent advances. A further problem is the very inadequate index. To give one example, this does not refer to sexual abuse, although this is to some extent dealt with under psychosexual disorders.

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